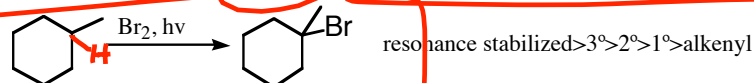
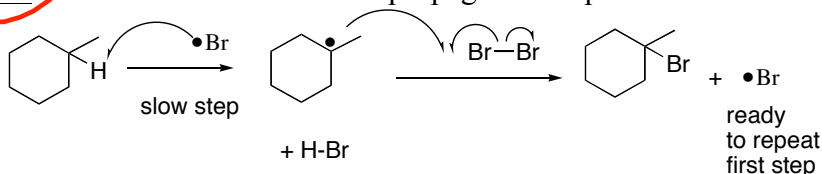
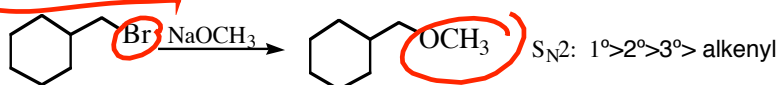
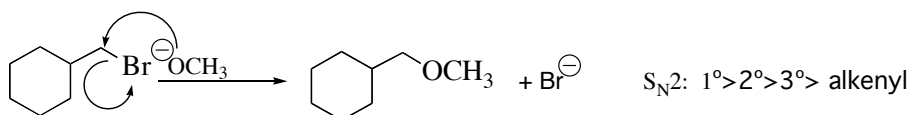


## Chem 350 Jasperse Ch. 6 Summary of Reaction Types, Ch. 4-6, Test 2

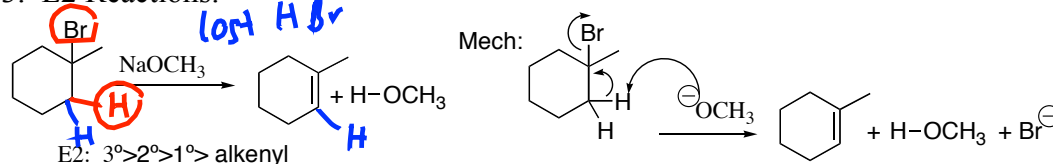
## 1. Radical Halogenation (Ch. 4)

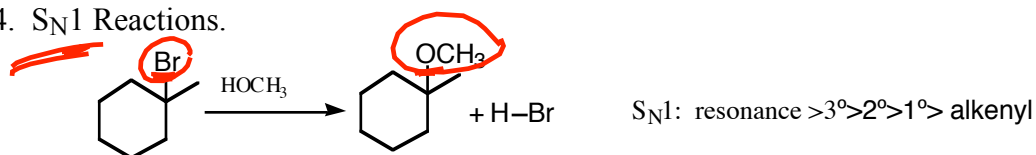
**Recognition:**  $X_2, hv$ **Predicting product:** Identify which carbon could give the most stable radical, and substitute a Br for an H on that carbon.**Stereochemistry:** Leads to racemic, due to achiral radical intermediate.**Mech:** Radical. Be able to draw propagation steps.2.  $S_N2$  Substitution

Any of a large variety of nucleophiles or electrophiles can work.

**Recognition:** A. Anionic Nucleophile, andB.  $1^\circ$  or  $2^\circ$  alkyl halide $(3^\circ$  alkyl halides fail, will give E2 upon treatment with Anionic Nucleophile/Base. For  $2^\circ$  alkyl halides,  $S_N2$  is often accompanied by variable amounts of E2.)**Predicting product:** Replace the halide with the anion nucleophile**Stereochemistry:** Leads to Inversion of Configuration**Mech:** Be able to draw completely. Only one concerted step!

## 3. E2 Reactions.

**Recognition:** A. Anionic Nucleophile/Base, andB.  $3^\circ$  or  $2^\circ$  alkyl halide $(1^\circ$  alkyl halides undergo  $S_N2$  instead. For  $2^\circ$  alkyl halides, E2 is often accompanied by variable amounts of  $S_N2$ .)**Orientation:** The most substituted alkene forms (unless a bulky base is used, ch. 7)**Predicting product:** Remove halide and a hydrogen from the neighboring carbon that can give the most highly substituted alkene. The hydrogen on the neighboring carbon must be trans, however.**Stereochemistry:** Anti/trans elimination. The hydrogen on the neighbor carbon must be trans/anti.**Mech:** Concerted. Uses anion. Be able to draw completely. Only one concerted step!

4.  $S_N1$  Reactions.

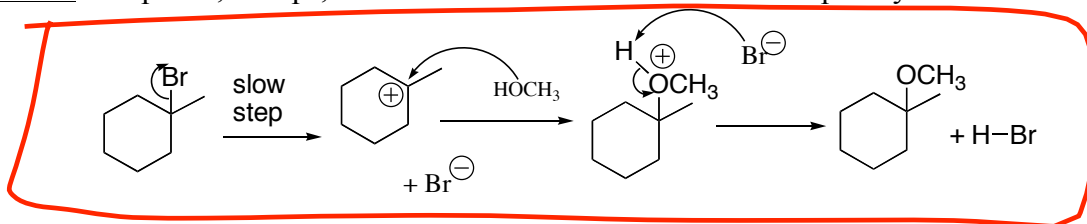
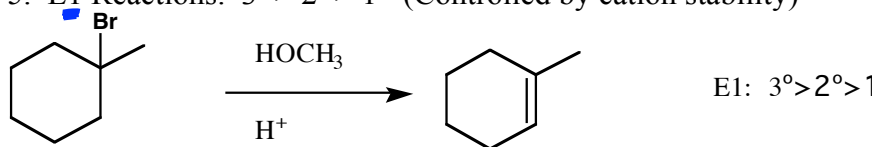
**Recognition:** A. Neutral, weak nucleophile. No anionic nucleophile/base, and  
B.  $3^\circ$  or  $2^\circ$  alkyl halide. (Controlled by cation stability).

( $1^\circ$  alkyl halides undergo  $S_N2$  instead. For  $2^\circ$  alkyl halides,  $S_N1$  is often accompanied by variable amounts of E1.)

**Predicting product:** Remove halide and replace it with the nucleophile (minus an H atom!)

**Stereochemistry:** Racemization. The achiral cation intermediate forgets any stereochem.

**Mech:** Stepwise, 3 steps, via carbocation. Be able to draw completely.

5. E1 Reactions.  $3^\circ > 2^\circ > 1^\circ$  (Controlled by cation stability)

**Recognition:** A. Neutral, weak nucleophile. No anionic nucleophile/base, and  
B.  $3^\circ$  or  $2^\circ$  alkyl halide. (Controlled by cation stability).

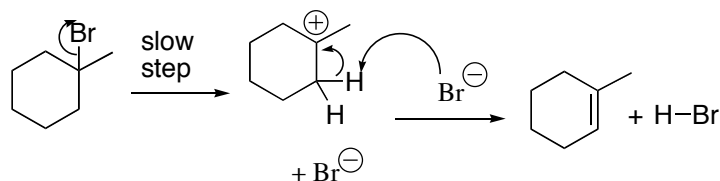
(For  $2^\circ$  alkyl halides, E1 is often accompanied by variable amounts of  $S_N1$ .)

**Orientation:** The most substituted alkene forms

**Predicting the major product:** Remove halide and a hydrogen from the neighboring carbon that can give the most highly substituted alkene. The hydrogen on the neighboring carbon can be cis or trans.

**Stereochemistry:** Not an issue. The eliminating hydrogen can be cis or trans.

**Mech:** Stepwise, 2 steps, via carbocation. Be able to draw completely.



Sorting among  $S_N2$ ,  $S_N1$ , E2, E1: How do I predict?

Step 1: **Check nucleophile/base.**

- If **neutral**, then  $S_N1/E1 \rightarrow$  mixture of both
- If **anionic**, then  $S_N2/E2$ .

Step 2: If **anionic**, and in the  $S_N2/E2$ , then **Check the substrate.**

- $1^\circ \rightarrow S_N2$
- $2^\circ \rightarrow S_N2/E2$  mixture. Often more  $S_N2$ , but not reliable...
- $3^\circ \rightarrow E2$

## Ch. 6 Alkyl Halides: Nucleophilic Substitution and Elimination

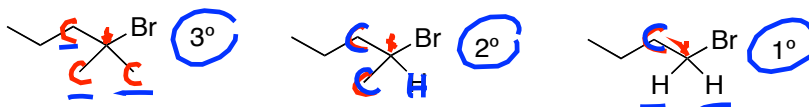
### 6.1,2 Classification, Nomenclature

#### A. General Classification

"alkyl halide"	halide connected to an $sp^3$ (alkyl) carbon	
"vinyl halide"	" $sp^2$ (vinyl $\approx$ alkenyl)	
"aryl halide"	"aromatic" ( $sp^2$ )	
"allylic halide"		

do not do  $S_N2$   $S_N1$   $E2$  or  $E1$

#### B. 1°, 2°, 3° Classification



#### C. Systematic Naming: x-Haloalkane (test responsible) (Include number!)

#### D. Common Naming: "alkyl halide" (not tested)

Structure	Formal Name	Common Name
	1-chloropropane	propyl chloride
	2-bromopentane	—
	2-iodopropane	isopropyl iodide

Systematic Nomenclature: x-Haloalkane (test responsible)

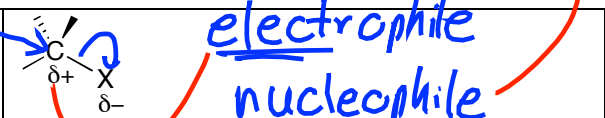
Common: "alkyl halide" (not tested)

#### Uses:

1. solvents
2. anesthetics
3. refrigerants
4. pesticides

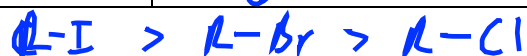
5. reactants

## 6.4 Structure:

A. Polar		
----------	--	--

B. Weak Bonds, Breakable

<u>Stability</u>	Bond	Bond Strength	<u>Reactivity Toward Breakage</u>
↑	C-Cl	81	
↑	C-Br	68	↓
↑	C-I	53	↓



## 6.5 Physical Properties

- boiling point: controlled by molecular weight (London force)
- water solubility: low, no hydrogen-bonding
- density: greater than water, so they sink (unlike hydrocarbons, which float)

## 6.6 Preparation of Alkyl Halides

- Review:  $R-H + Br_2 \xrightarrow{h\nu} RBr + HBr$  (under photolysis, Ch. 4)
- We will learn other preparations in chapters 8 and 11

## 6.7 Basic Overview/Preview of Alkyl Halide Reactions: Substitution (S<sub>N</sub>2 or S<sub>N</sub>1) or Elimination (E2 or E1)

- Because R-X bonds are weak, halides are good leaving groups.

### E. Substitution

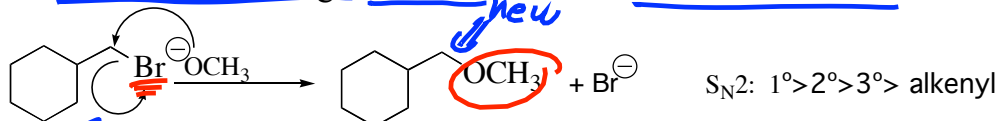


Anion or neutral

2 Variants

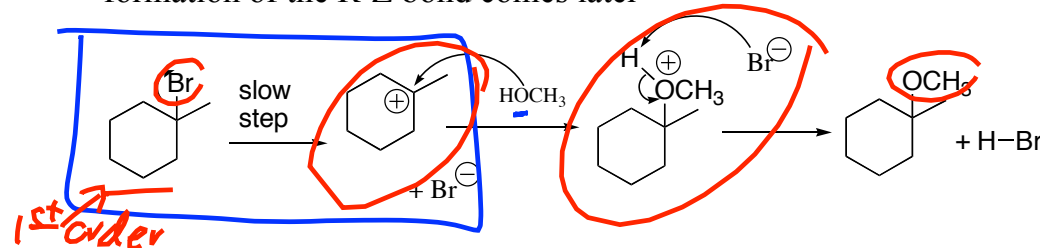
6. S<sub>N</sub>2

- Anionic nucleophile
- The R-X bond breaking is simultaneous with R-Z bond formation

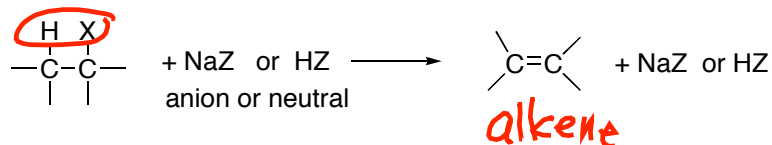


7. S<sub>N</sub>1:

- Neutral nucleophile
- The R-X bond breaks first to give a carbocation in the rate determining step; formation of the R-Z bond comes later



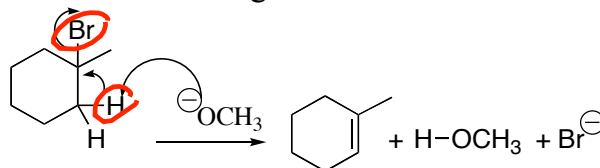
### F. Elimination



2 Variants

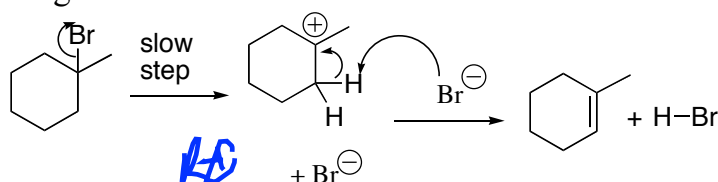
1. E2:

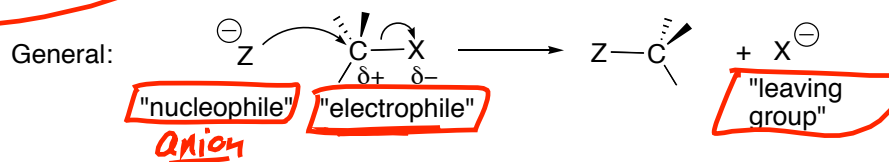
- Anionic base
- The R-X and C-H bond breaking is simultaneous with C=C bond formation



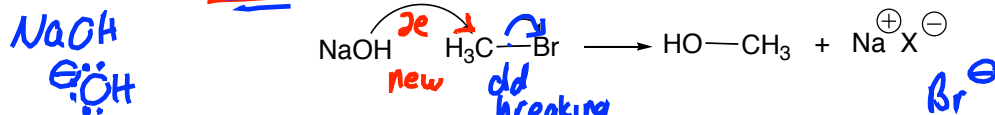
2. E1:

- Neutral base
- The R-X bond breaks first to give a carbocation in the rate determining step. C-H bond cleavage and C=C bond formation comes later



68 The S<sub>N</sub>2 Reaction

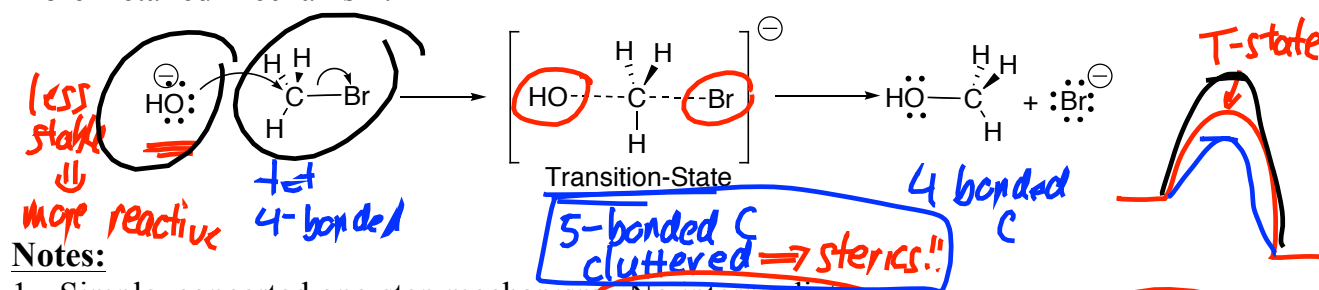
Example, with test-level mechanism:



- double-barbed arrows (electron pairs move)
- $\text{Na}^+$  is a spectator

Double-barbed arrows only. No arrows to Na or from Na. Deal with covalent bonds only.

More Detailed Mechanism:



Notes:

- Simple, concerted one-step mechanism. **No intermediates.**
- The anion needs to be very reactive and thus not too stable. Normally **ANIONIC NUCLEOPHILE**.
- Both nucleophile and electrophile are involved in the rate determining step.
  - Rate =  $k[\text{anion}]^1[\text{R-X}]^1$
- 2<sup>nd</sup> order rate law** is why it's called S<sub>N</sub>2: **Substitution<sub>Nucleophilic</sub> 2<sup>nd</sup> order**
- The nucleophile attacks **opposite side from the leaving group**.
- This "backside attack" (or **opposite side attack**) results in **inversion** of stereochemistry when a **chiral, 2° R-X** is involved



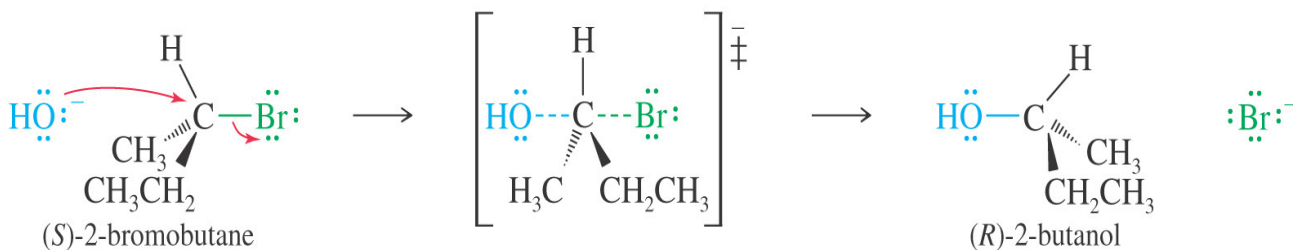
- The **transition state** involves a **5-bonded, trigonal bipyramidal carbon** that **is more cluttered** than either the original tetrahedral reactant or the final tetrahedral product
- Steric crowding** in the transition-state makes the reaction **very, very, very sensitive to steric factors**

- For the electrophile R-X:  $\text{CH}_3-\text{X} > 1^\circ \text{R-X} > 2^\circ \text{R-X} > 3^\circ \text{R-X}$  for steric reasons
- For the nucleophile it also helps to be smaller rather than larger

**3° R-X**  
 $\downarrow$   
**No S<sub>N</sub>2**

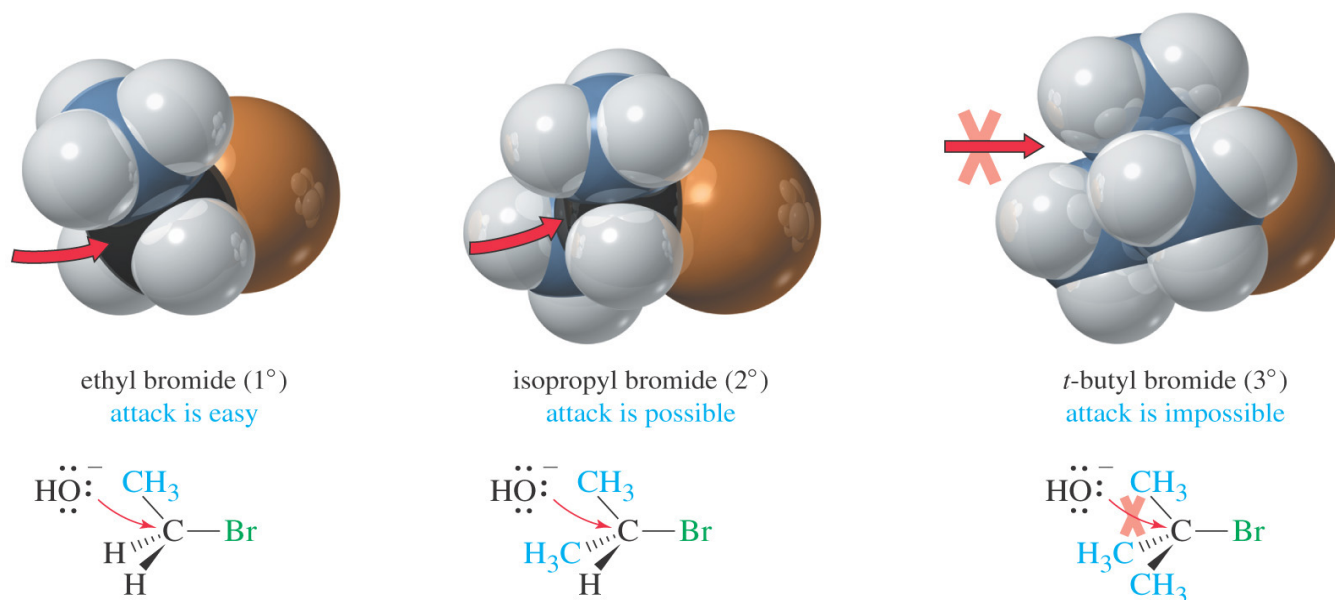
## Mechanism

1. Crowded transition state (sterics are crucial)
2. 2nd order (SN2)
3. Opposite-side attack => inversion



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Steric Factor: methyl > primary > secondary >>> tertiary (can't work)



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6.9 Generality of S<sub>N</sub>2 Reactions

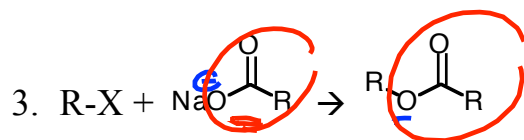
-many kinds of nucleophiles, give many products



Alcohols



Ethers



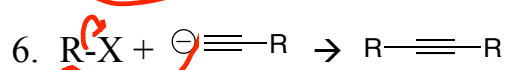
Esters



Iodides



Nitriles



Alkynes

Etc.

## Notes

1. Most nucleophiles are **ANIONS**

2. Various oxygen anions are good to make alcohols, ethers, or esters

3. Halogen exchange useful route to iodides (more valuable and less accessible)

4. There are a few neutral nucleophiles (not for test): nitrogen family

Predicting Products for S<sub>N</sub>2 Reactions

1. Don't change the structure for the carbon skeleton

2. Put the nucleophile in exactly the spot where the halide began...

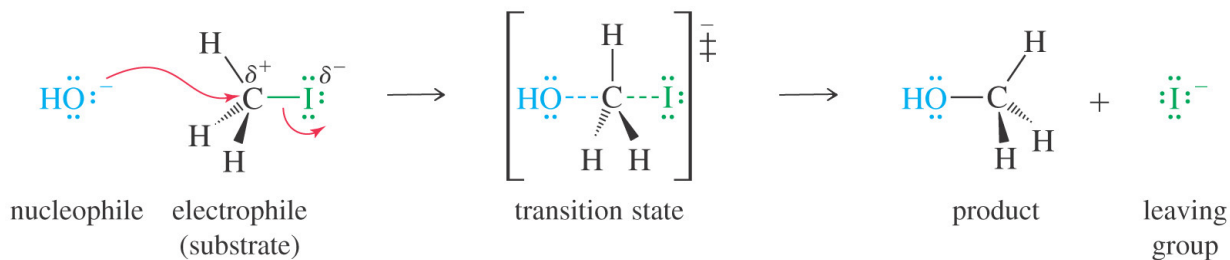
3. Unless the halide was attached to a **chiral** center; in that case invert the configuration for the product

- If the halide was "wedged", the nucleophile should be "hashed"

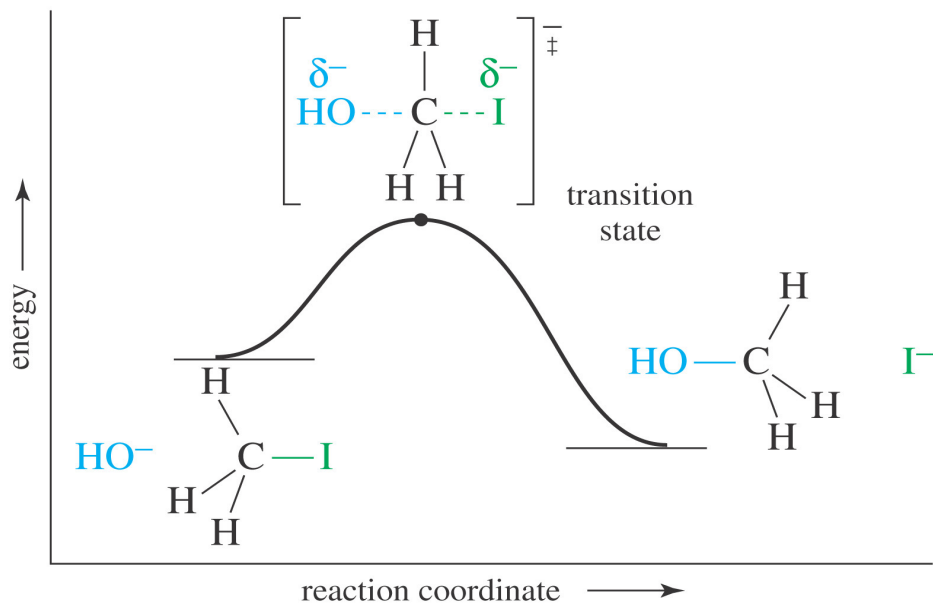
- If the halide was "hashed", the nucleophile should be "wedged"

4. Don't mess with any "spectator" portions: whatever was attached to the nucleophilic anion at the beginning should still be attached at the end





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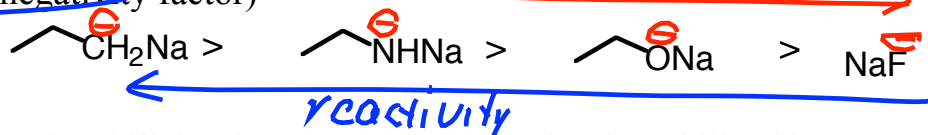
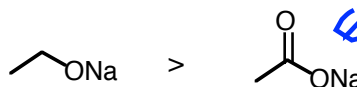


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Nucleophile		Product	Class of Product
$\text{R-X} + \text{:}\ddot{\text{I}}\text{:}$	$\longrightarrow$	$\text{R}-\ddot{\text{I}}\text{:}$	alkyl halide
$\text{R-X} + \text{:}\ddot{\text{O}}\text{H}^-$	$\longrightarrow$	$\text{R}-\ddot{\text{O}}\text{H}$	alcohol
$\text{R-X} + \text{:}\ddot{\text{O}}\text{R}'^-$	$\longrightarrow$	$\text{R}-\ddot{\text{O}}\text{R}'$	ether
$\text{R-X} + \text{:}\ddot{\text{S}}\text{H}^-$	$\longrightarrow$	$\text{R}-\ddot{\text{S}}\text{H}$	thiol (mercaptan)
$\text{R-X} + \text{:}\ddot{\text{S}}\text{R}'^-$	$\longrightarrow$	$\text{R}-\ddot{\text{S}}\text{R}'$	thioether (sulfide)
$\text{R-X} + \text{:NH}_3$	$\longrightarrow$	$\text{R}-\text{NH}_3^+ \text{X}^-$	amine
$\text{R-X} + \text{:}\ddot{\text{N}}=\text{N}^+=\ddot{\text{N}}\text{:}^-$	$\longrightarrow$	$\text{R}-\ddot{\text{N}}=\text{N}^+=\ddot{\text{N}}\text{:}^-$	azide
$\text{R-X} + \text{:C}\equiv\text{C-R}'$	$\longrightarrow$	$\text{R}-\text{C}\equiv\text{C-R}'$	alkyne
$\text{R-X} + \text{:C}\equiv\text{N:}$	$\longrightarrow$	$\text{R}-\text{C}\equiv\text{N:}$	nitrile
$\text{R-X} + \text{R}'-\text{CO}\ddot{\text{O}}\text{:}^-$	$\longrightarrow$	$\text{R}'-\text{COO-R}$	ester
$\text{R-X} + \text{:P(Ph)}_3$	$\longrightarrow$	$[\text{R}-\text{PPh}_3]^+ \text{X}^-$	phosphonium salt

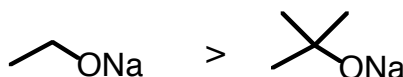
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6.10-6.11 Structural Factors that Impact  $S_N2$ **A. Nucleophile**1. Anion versus Neutral: Should be **ANIONIC** $HO^-$  less stable  $\Rightarrow$  more reactive  $H_2O$ 2. Anion Stability: Less Stable should be More Reactive (Reactant Stability-Reactivity Principle)a. -anion nucleophilicity decreases across a **horizontal row** (electronegativity factor)b. -anion nucleophilicity decreases when an anion is stabilized by **resonance**

↓ less reactive

c. -anion nucleophilicity increases down a **vertical column**

3. Size: all else equal, smaller is better than bigger

**B. Electrophile**1. **Substrate:** Allylic >  $1^\circ$  >  $2^\circ$  > >>  $3^\circ$ , alkenyl, aryl

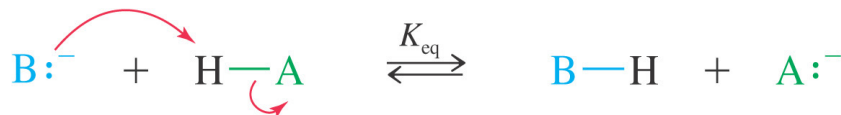
- **$3^\circ$  and alkenyl, aryl never do  $S_N2$**
- transition-state stability-reactivity principle
- Steric clutter in the transition state explains the  $1^\circ > 2^\circ > >> 3^\circ$  pattern
- Allylic benefits from a complex orbital resonance effect in the T-state
- Alkenyl/aryl halides are bad for some molecular orbital reasons (backside attack doesn't work, particularly for aryl halides)

2. **Leaving Group:** R-I > R-Br > R-Cl

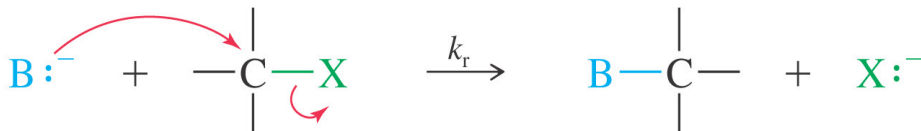
- reactant stability-reactivity principle
- weaker bonds break faster

Analogy: Anions as Bases, Anions as Nucleophiles.  
 Factors that make an anion less stable make it more reactive as both a base and as a nucleophile. (normally....)

### Basicity



### Nucleophilicity

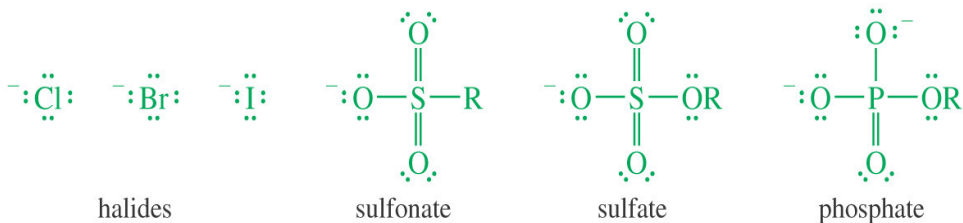


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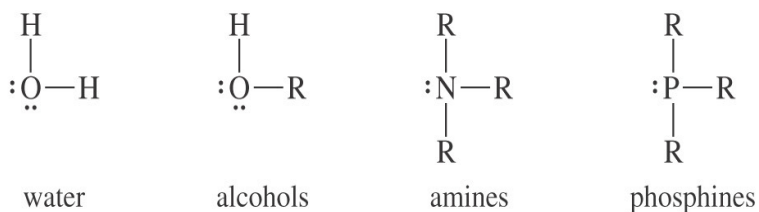
### Various Leaving Groups.

- Halides are good, but not the only leaving groups.
- The more stable something is after it leaves, the better it is as a leaving group.
  - the halide anions are like what you'd get from HCl, HBr, HI (strong acids).
  - the sulfonates are like what you'd get from sulfuric acid (strong acid)
  - water is like what you'd get from hydronium (strong acid)
- Notice that things were one charge unit more positive with one extra bond before they actually left.
  - to get H<sub>2</sub>O off, you'd have had charge ROH<sub>2</sub> (cation) first.
  - From a neutral alcohol, the leaving group would be hydroxide (bad), not water

Ions:

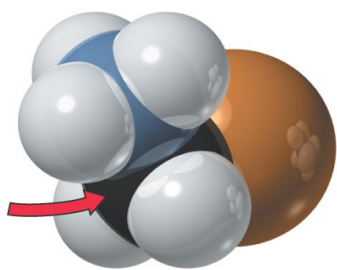


Neutral molecules:

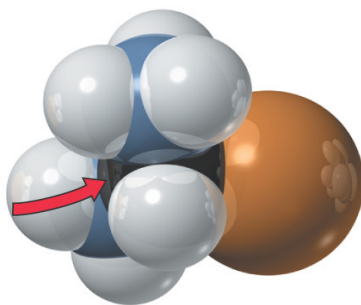
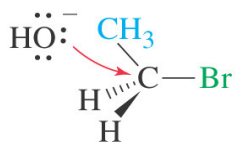


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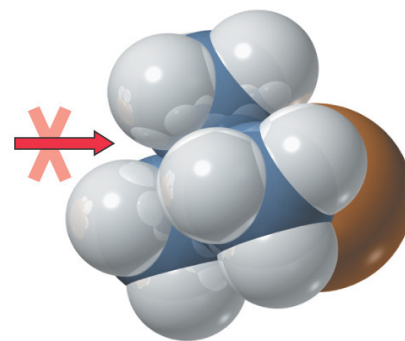
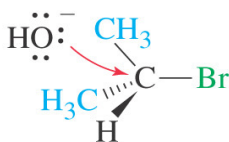
Steric Factor: primary > secondary >>> tertiary



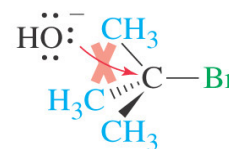
ethyl bromide (1°)  
attack is easy



isopropyl bromide (2°)  
attack is possible

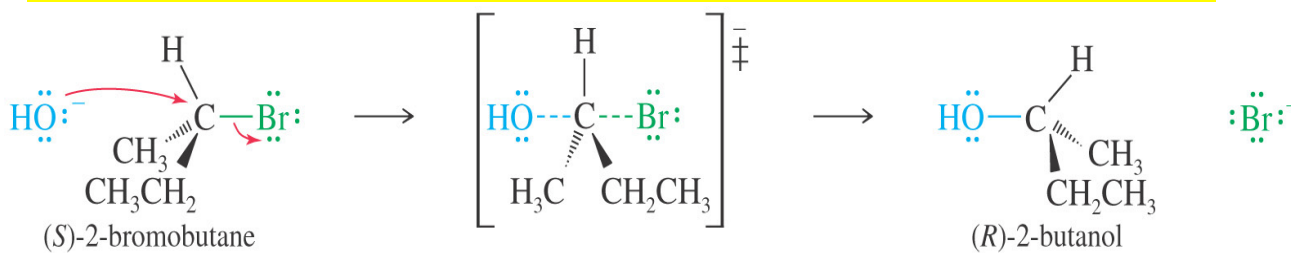


*t*-butyl bromide (3°)  
attack is impossible



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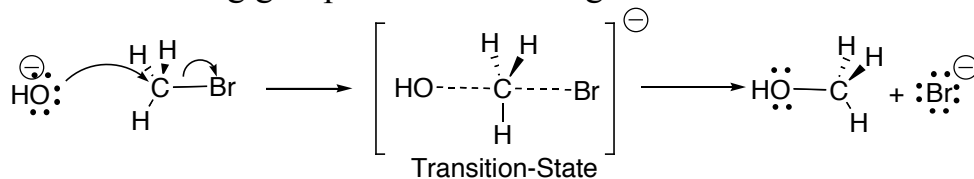
1. Crowded Transition-state. Sterically sensitive
2. Inversion of stereochemistry



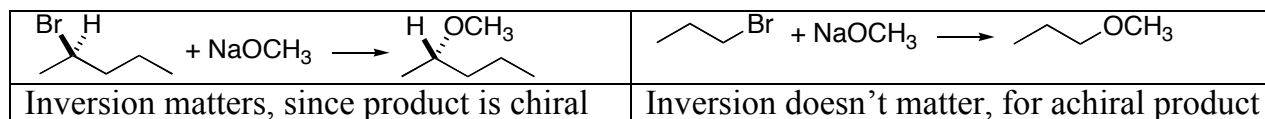
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6.12 Inversion of Stereochem in  $S_N2$ 

In the mechanism, the nucleophile attacks from the “backside” or opposite side from the leaving group  $\rightarrow$  inverts configuration

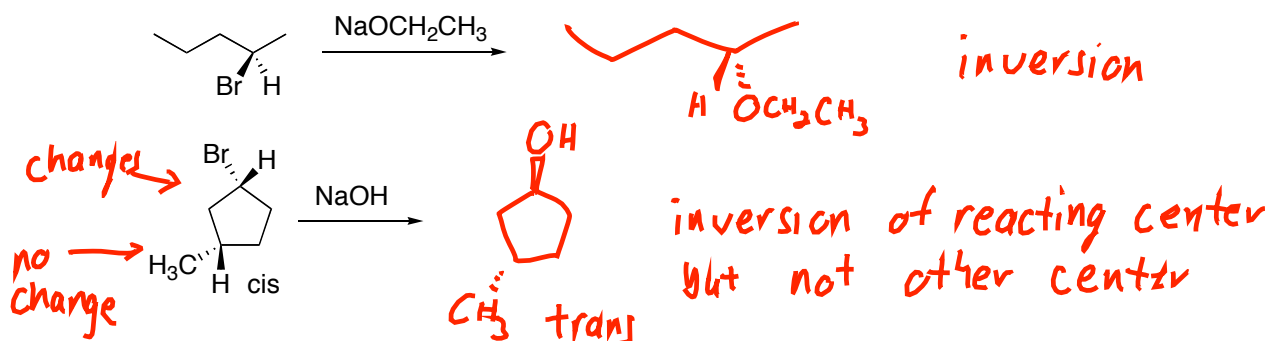


- Inversion occurs mechanistically in **every**  $S_N2$  reaction
- But inversion is chemically relevant **only** when a chiral carbon is involved



Predicting products when chiral carbons undergo inversion:

1. Keep the carbon skeleton fixed
2. If leaving group is “hashed”, the nucleophile will end up “wedged” in the product
3. If leaving group is “wedged”, the nucleophile will end up “hashed” in the product



Two Standard Proofs for  $S_N2$  mechanism:

- Inversion of configuration on a chiral carbon
- 2<sup>nd</sup> order rate law

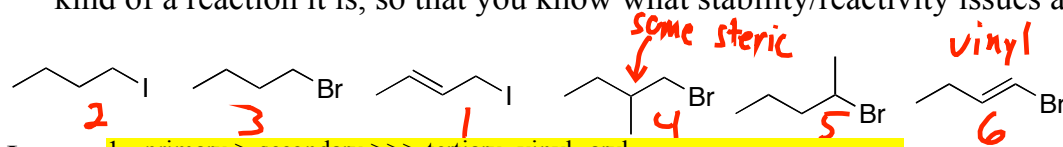
Predicting Products for  $S_N2$  Reactions

1. Don't change the structure for the carbon skeleton
2. **Put the nucleophile in exactly the spot where the halide began...**
3. Unless the halide was attached to a **chiral** center; in that case invert the configuration for the product
  - a. If the halide was “wedged”, the nucleophile should be “hashed”
  - b. If the halide was “hashed”, the nucleophile should be “wedged”
4. Don't mess with any “spectator” portions: whatever was attached to the nucleophilic anion at the beginning should still be attached at the end



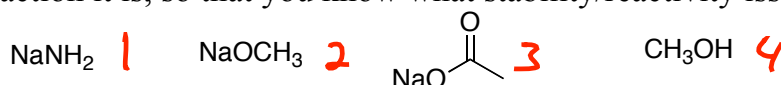
More S<sub>N</sub>2 Problems

1. Rank the reactivity toward NaOCH<sub>3</sub> (For any problem like this, try to recognize what kind of a reaction it is, so that you know what stability/reactivity issues apply).



- Issues:
1. primary > secondary >>> tertiary, vinyl, aryl
  2. RI > RBr > RCl
  3. Allylic > non-allylic
  4. Steric tiebreaker, all else equal

2. Rank Reactivity toward Br (For any problem like this, try to recognize what kind of a reaction it is, so that you know what stability/reactivity issues apply).

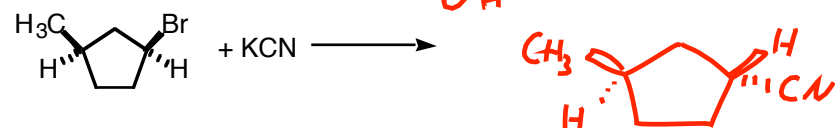
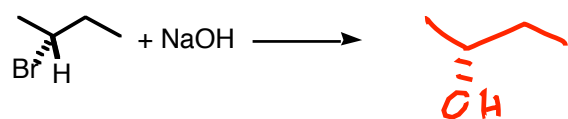


- Issues:
1. Charge: Anions > Neutral
  2. Electronegativity/periodic table: N > O
  3. Resonance stabilization reduces nucleophilic reactivity

3. What nucleophile should you use to accomplish the following transformations?

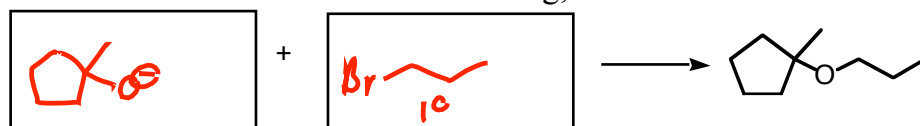


4. Draw the Products, Including Stereochemistry. (Stereochemistry will matter for S<sub>N</sub>2 and S<sub>N</sub>1 reactions anytime the haloalkane is 2°)



- Issue: Inversion of stereochemistry at reacting carbon

5. Choose Reactants to make the following, from a haloalkane and some nucleophile.



- Issues: *but not* +  $\ominus\text{O}-\text{CH}_2\text{CH}_2\text{CH}_3$  because 3° RBr

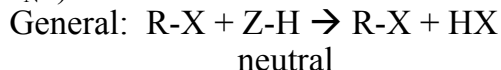
Electrophile RX needs to be methyl, primary, or secondary.

But it can't be tertiary, vinyl, or aryl.

In the problem shown, the "boxed" answers involve a primary RX. The "bad" answer has a tertiary RX.

6.13  $S_N1$  = Substitution<sub>Nucleophilic</sub>1st Order = "Solvolysis"

- Dramatic difference in mechanism, rates, structure dependence, and stereochemical outcome (compared to  $S_N2$ )



**Neutral, non-anionic** nucleophiles do the substitution

- Often this is just the solvent ( $H_2O$ ,  $ROH$ ,  $RCO_2H$  are common)
  - For this reasons, these reactions are often called "solvolysis" reactions
- Heat is often required
- Acid is sometimes used to accelerate  $S_N1$  reactions

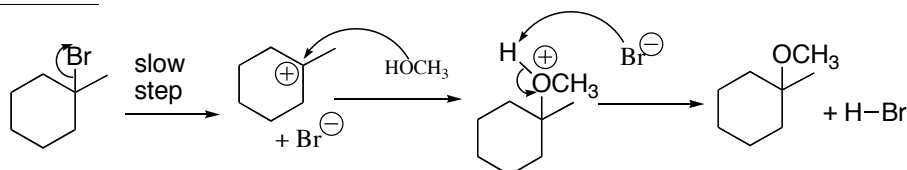
### Predicting Products for $S_N1$ Reactions

- Don't change the structure for the carbon skeleton
- Connect "R" and "Z", while taking the halide off of the electrophile and H off of the nucleophile
- Unless the halide was attached to a **chiral** center, a **racemic mixture** will result
- Maintain the integrity of the spectator attachments

Examples:



### 3-Step Mechanism



- Step 1: Carbocation Formation. **THIS IS THE SLOW STEP**

• **Therefore the rate is controlled by cation stability!**

- Step 2: Carbocation capture by neutral molecule (usually a solvent molecule)
  - When cation and neutral combine, a cation is produced
- Step 3: Deprotonation to get neutral

Notes:

- Carbocation formation is key
- Rate =  $k[R-X] \rightarrow$  First order
- See cations, not anions. Neutral, not anionic nucleophile.
- Charge and atoms must balance in step 2. Thus, the oxygen retains the hydrogen.
- Oxygen eventually loses the H, but only in step 3.
- Rate can be enhanced by  $AgNO_3$ . The  $Ag^+$  cation helps strip the halide off in step 1.


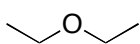
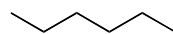


**Structural** Factors that Impact  $S_N1$  Rates

**Nucleophile:** Should be **NEUTRAL**, but otherwise non-factor

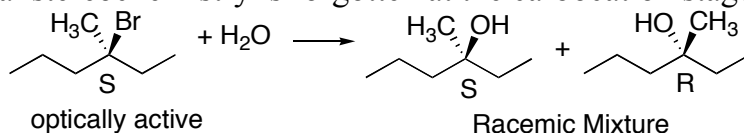
**Electrophile**

- Substrate: Allylic  $>$   $3^\circ >$   $2^\circ >$   $1^\circ >$  alkenyl, aryl
  - Resonance is huge
  - alkenyl, aryl never do  $S_N2$ ,  $1^\circ$  only with  $AgNO_3$
  - product stability-reactivity principle: in the rate-determining step, the more stable the product **cation**, the faster it will form
  - In terms of  $1^\circ$ ,  $2^\circ$ ,  $3^\circ$ ,  $S_N1$  and  $S_N2$  have exactly opposite patterns
- Leaving Group:  $R-I >$   $R-Br >$   $R-Cl$ 
  - reactant stability-reactivity principle: in the rate determining step, the weaker the C-X bond, the faster it will break
  - This pattern is the same as for  $S_N2$
- $AgNO_3$  Helps
  - $Ag^+$  helps strip the halide off in step one
- Polar Solvent Helps
  - A polar solvent helps to stabilize the ions that form in the rate-determining step

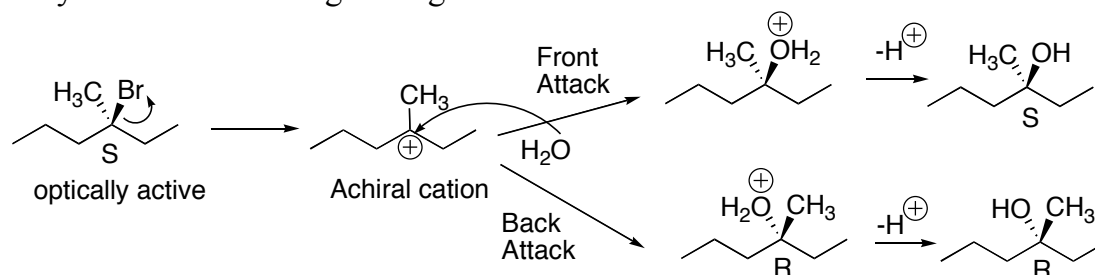
Solvent Polarity:					
Solvent	$H_2O$	$CH_3OH$			
Relative Rate	8000	1000	1	0.001	0.0001

6.14  $S_N1$  Stereo: Racemization

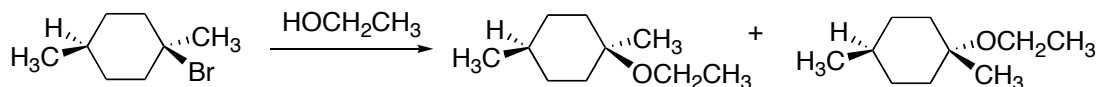
Original stereochemistry is forgotten at the carbocation stage, get racemic R/S mixture



Why? Carbocation forgets original stereo:

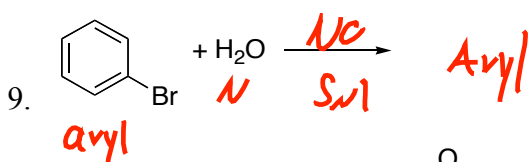
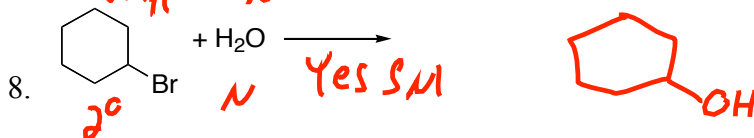
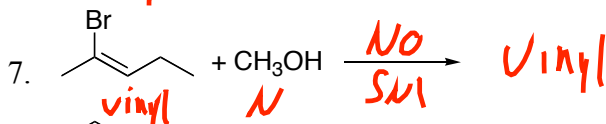
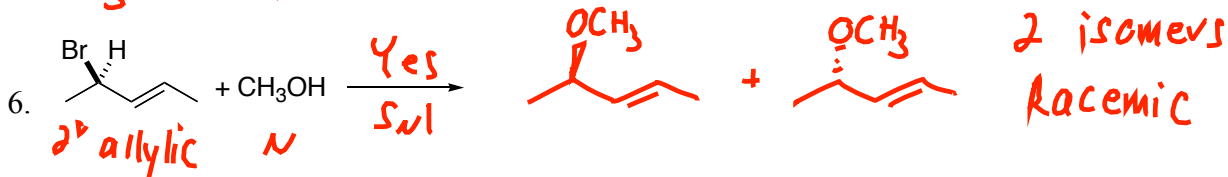
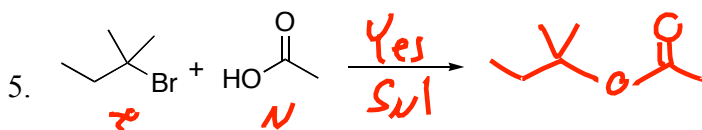
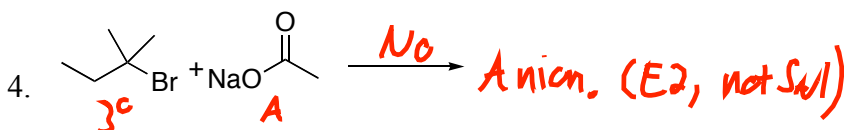
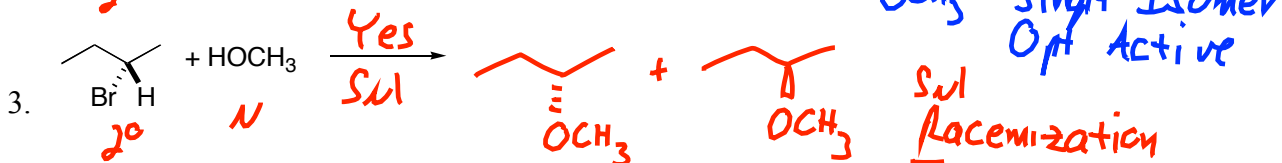
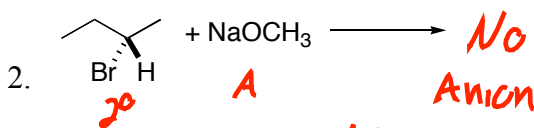
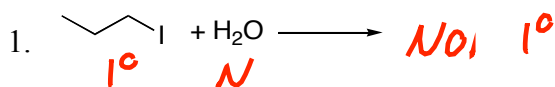


Ex.

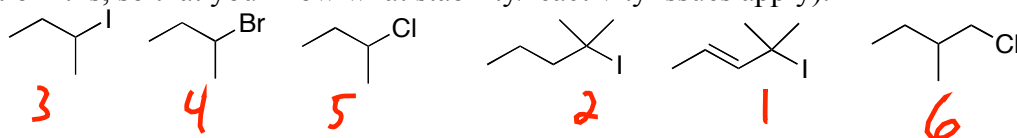


S<sub>N</sub>1 Problems: For the following, which are and aren't S<sub>N</sub>1 candidates? If not, why not? What would be the product if they are S<sub>N</sub>1 candidates?

1. Check nucleophile. Neutral or Anion?
2. Check Electrophile RX. Tertiary or secondary (S<sub>N</sub>1 OK). Primary, vinyl, or aryl no S<sub>N</sub>1.



10. Rank Reactivity towards (For any problem like this, try to recognize what kind of a reaction it is, so that you know what stability/reactivity issues apply).



Issues:

1. Tertiary > secondary >>>>>> primary, vinyl, aryl
2. RI > RBr > RCl
3. Allylic > non-allylic

6.16 Comparing  $S_N2$  vs  $S_N1$ 

		$S_N1$	$S_N2$
1	Nucleophile	Neutral, weak	Anionic, strong
2	Substrate	$3^\circ R-X > 2^\circ R-X$	$1^\circ R-X > 2^\circ R-X$
	Allylic effect...	Allylic Helps	Allylic helps
3	Leaving Group	$I > Br > Cl$	$I > Br > Cl$
4	Solvent	Polar needed	Non-factor
5	Rate Law	$k[RX]$	$k[RX][Anion]$
6	Stereochemistry (on chiral, normally $2^\circ R-X$ )	Racemization	Inversion
7	Ions	Cationic	Anionic
8	Rearrangements	Problem at times	Never

Identify as  $S_N1$  or  $S_N2$  or No Reaction. Draw the Product(s), if a reaction occurs.

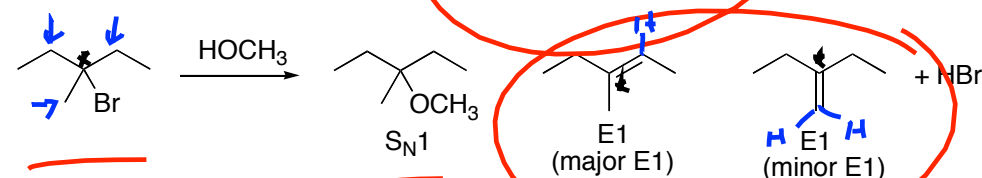
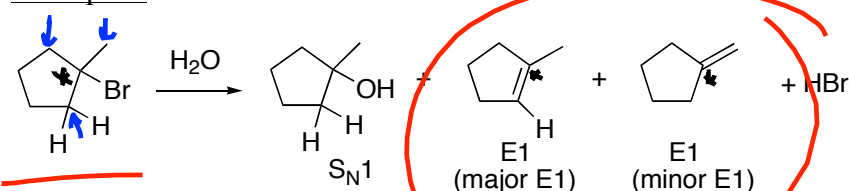
1.  $CH_3CH_2CH_2Br + NaOCH_2CH_3 \rightarrow$   $S_N2$   
 $1^\circ$   $A$   $CH_3CH_2CH_2OCH_2CH_3$
2.  $C_6H_5Br + H_2O \rightarrow$  No Reaction  
 $aryl$   $N$
3.  $C_6H_{11}Br + H_2O \rightarrow$   $S_N1$   
 $3^\circ$   $N$   $C_6H_{11}OH$
4.  $CH_3CH(Br)CH_2CH_3 + CH_3SNa \rightarrow$   $S_N2$   
 $2^\circ$   $A$   $CH_3CH(SCH_3)CH_2CH_3$  inversion, 1 isomer, opt. active
5.  $CH_3CH(Br)CH_2CH_3 + CH_3SH \rightarrow$   $S_N1$   
 $2^\circ$   $N$   $CH_3CH(SCH_3)CH_2CH_3$  +  $CH_3CH(SCH_3)CH_2CH_3$  racemization, 2 isomers, racemic

Which fit  $S_N1$ , which fit  $S_N2$ ?

- Faster in presence of silver nitrate?  $S_N1$
- Faster in water than in hexane?  $S_N1$
- When the moles of reactant is kept the same, but the volume of solvent is cut in half, the reaction rate increases by 2-fold?  $S_N1$
- By 4-fold?  $S_N2$
- 2-bromobutane reacts faster than 1-bromobutane?  $S_N1$
- 2-bromobutane reacts slower than 1-bromobutane?  $S_N2$

## 6-17 E1 Elimination Reactions

## Examples.



## Notes

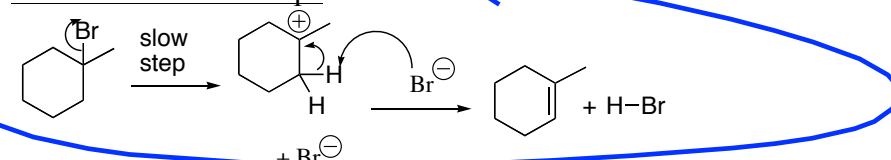
- Under  $\text{S}_{\text{N}}1$  conditions, some elimination product(s) form as well
- E1 and  $\text{S}_{\text{N}}1$  normally compete, resulting in mixtures
  - This is not good from a synthetic perspective.

## • Structurally Isomeric Alkenes can form

- The double bond must involve the original halogenated carbon and any neighbor carbon (that had a hydrogen to begin with that can be eliminated)
- Normally the alkene with fewer alkene H's is formed more extensively over alkenes with more alkene H's. (More C-substituted alkene is major).

- Neutral/acidic (the formula starts neutral, but acid is produced)
- 1<sup>st</sup> order rate law  $r = k[\text{RX}]^1$

## E1 Mechanism: 2 Steps



1. Step 1: Carbocation Formation. THIS IS THE SLOW STEP
  - a. Therefore the rate is controlled by cation stability! Just like  $\text{S}_{\text{N}}1$ !
  - b. Benefits from exactly the same factors that speed up  $\text{S}_{\text{N}}1$  ( $3^\circ > 2^\circ$ , RI > RBr, polar solvent, etc..)
2. Step 2: Deprotonation from a carbon that neighbors the cation/original halogenated carbon
  - a. Can draw bromide as base for simplicity
  - b. But often it's actually water or alcohol solvent that picks up the proton

## E1 Summary

**Recognition:** A. Neutral, weak nucleophile. No anionic nucleophile/base, and B.  $3^\circ$  or  $2^\circ$  alkyl halide. (Controlled by cation stability).

(For  $2^\circ$  alkyl halides, E1 is often accompanied by variable amounts of  $\text{S}_{\text{N}}1$ .)

**Orientation:** The most substituted alkene forms

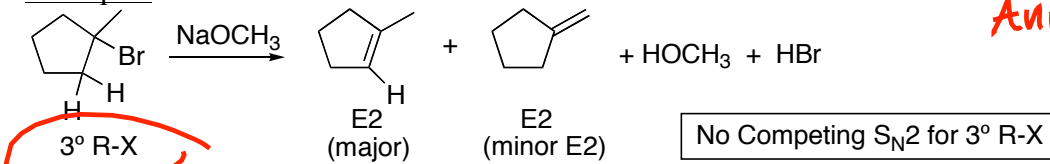
**Predicting the major product:** Remove halide and a hydrogen from the neighboring carbon that can give the most highly substituted alkene. The hydrogen on the neighboring carbon can be cis or trans.

**Stereochemistry:** Not an issue. The eliminating hydrogen can be cis or trans. .

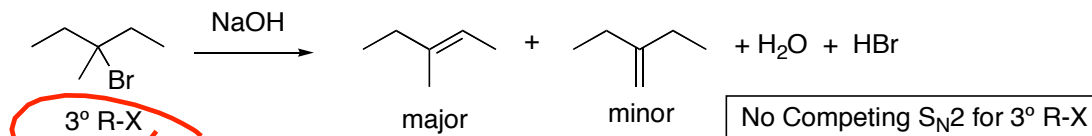
**Mech:** Stepwise, 2 steps, via carbocation. Be able to draw completely.

6-19 E2 Reaction (2<sup>nd</sup> Order, Under Anionic/Basic S<sub>N</sub>2 type Conditions)

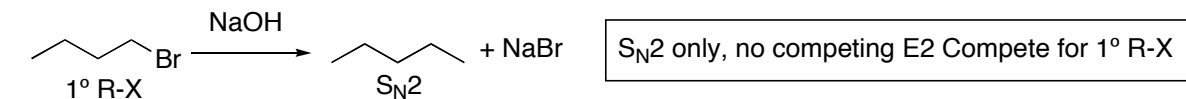
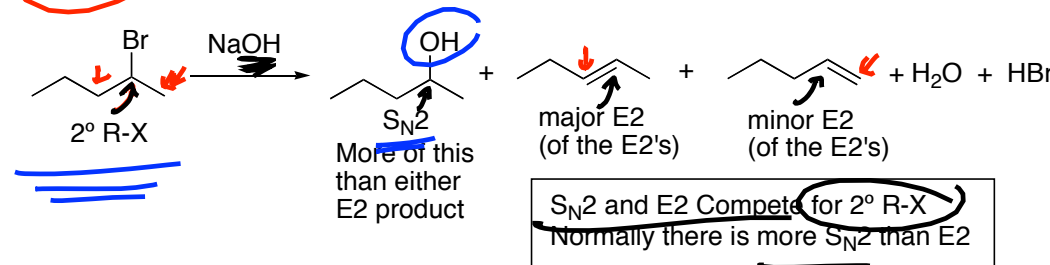
Examples



Anionic 3° R-X  
E2 only



~~80%~~ S<sub>N</sub>2  
2° and E2



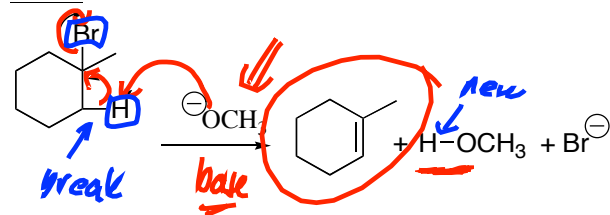
1° S<sub>N</sub>2 only

Notes

- E2 happens with anionic nucleophiles/bases, when S<sub>N</sub>2 is hindered
- Structurally Isomeric Alkenes can form

- The double bond must involve the original halogenated carbon and any neighbor carbon (that had a hydrogen to begin with that can be eliminated)
- Normally the alkene with fewer alkene H's is formed more extensively over alkenes with more alkene H's. (More C-substituted alkene is major).

Mech



All changes happen at once  
"concerted"

- anionic. Anion base gets things started.
- 2<sup>nd</sup> order rate law. Rate = k[R-X][anion base]<sup>1</sup>
- It all happens in one concerted step, but there are three arrows to show all the bond making and breaking

Bonds Made	Bonds Broken
Base to hydrogen	C-X bond
C=C pi bond	C-H bond

## E2 Summary

**Recognition:** A. Anionic Nucleophile/Base, and  
B. 3° or 2° alkyl halide

(1° alkyl halides undergo SN2 instead. For 2° alkyl halides, E2 is often accompanied by variable amounts of SN2.)

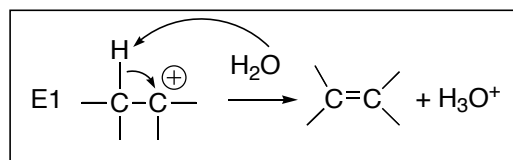
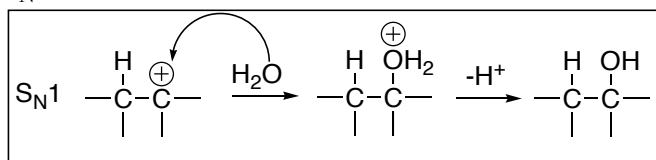
**Orientation:** The most substituted alkene forms (unless a bulky base is used, ch. 7)

**Predicting product:** Remove halide and a hydrogen from the neighboring carbon that can give the most highly substituted alkene. The hydrogen on the neighboring carbon must be trans, however.

**Stereochemistry:** Anti elimination. The hydrogen on the neighbor carbon must be trans/anti.

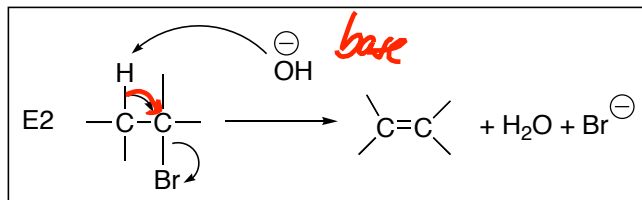
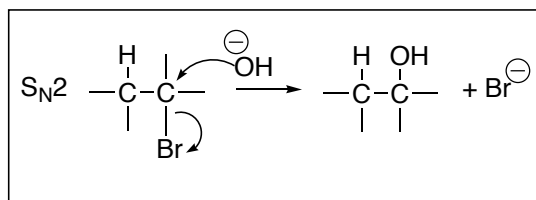
**Mech:** Concerted. Uses anion. Be able to draw completely. Only one concerted step!

## SN1 vs E1



- Both satisfy the carbocation. They just meet it's bonding need with different electrons.

## SN2 vs E2



- Both provide an electron pair to displace the C-Br bond pair. They just use different electrons.
- Both involve the anion. It's called the nucleophile in the SN2, the base in the E2.
- The SN2 involves a crowded transition state, and thus is strongly impacted by steric factors. The E2 does not have any steric problems (and in fact alleviates them).
- The difference in steric profile explains why for SN2, 1° > 2° > 3°, but that for E2, the reactivity of 3° is just fine.



6-18 Zaitsev's Rule: When E1 or E2 elimination can give more than 1 structurally isomeric alkene, **the more highly Carbon-substituted alkene form will predominate over a less highly carbon-substituted alkene.**

a. **The fewer H's on the product alkene the better.**

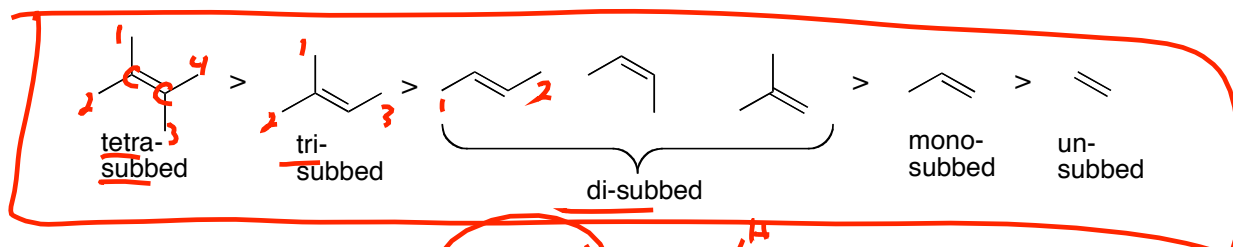
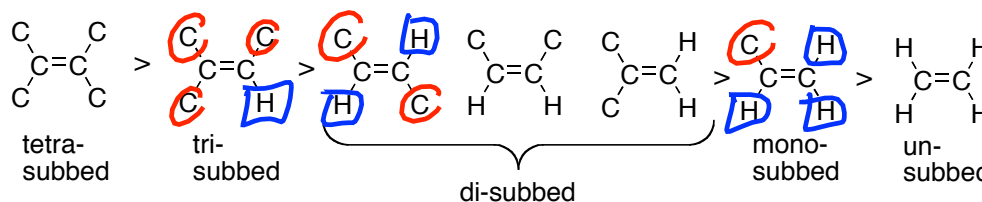
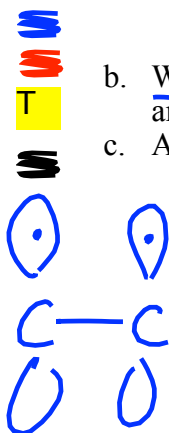
- Every Alkene has four attachments. The fewer of these that are H's, the better.
- When pictures are drawn in which the H's are not shown, the more highly substituted alkenes turn out to be the best.

b. **Why? Product Stability-Reactivity Rule.** Alkenes with more C's and fewer H's attached are more stable.

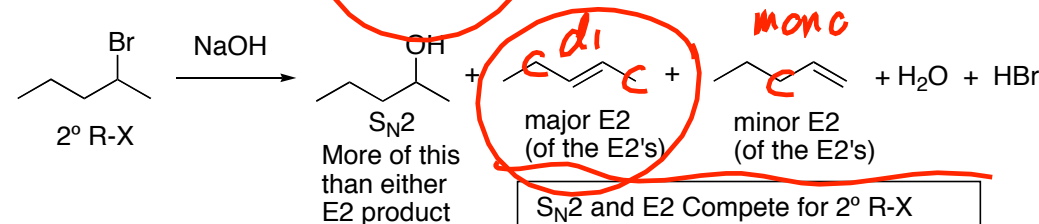
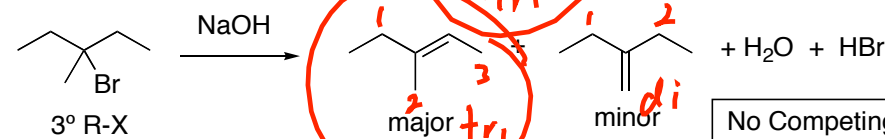
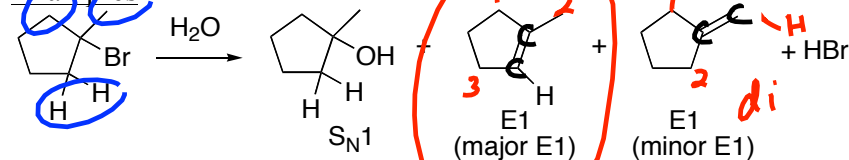
c. Alkene Stability is shown below: tetra- > tri- > di- > mono- > unsubstituted

○ Why?

- Alkene carbons are somewhat electron poor due to the inferior overlap of pi bonds. (One carbon doesn't really "get" as much of the other carbon's electron as is the case in a nice sigma bond).
- Since alkyl groups are electron donors, they stabilize electron-deficient alkene carbons.
- Analogous to why electron-donating alkyls give the  $3^\circ > 2^\circ > 1^\circ$  stability pattern for cations and radicals

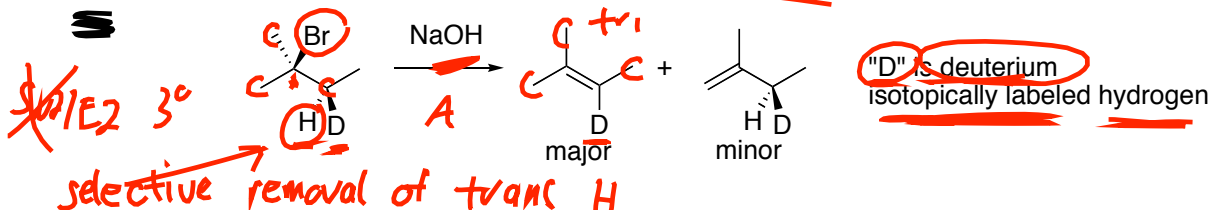


Examples

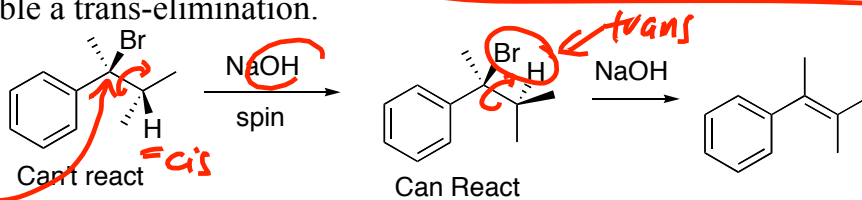


**Stereochemistry of E2 Eliminations (6.20)**

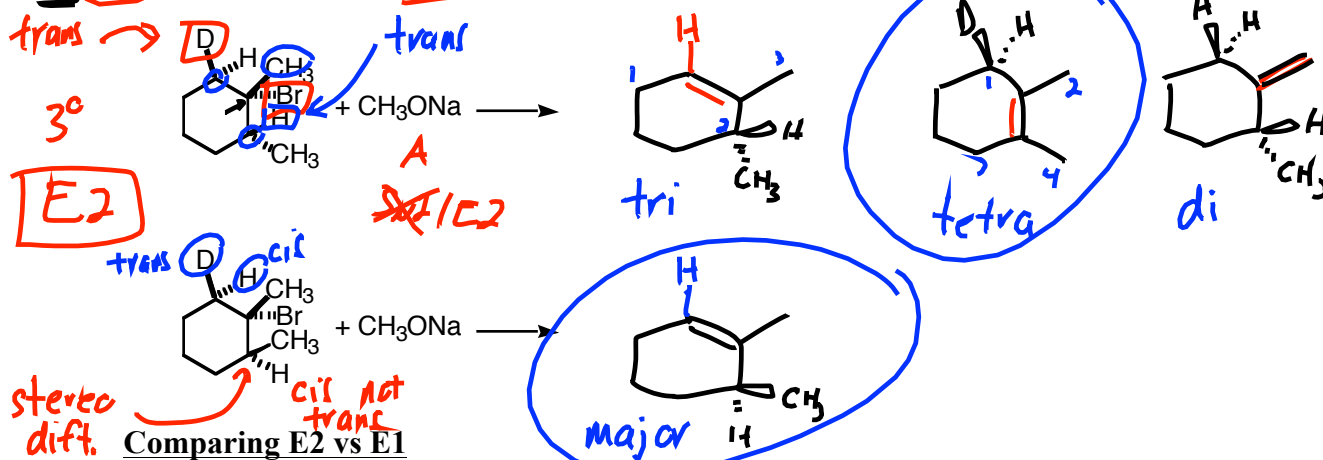
- For E2 (not for E1) C-H and C-X bonds must be in the same plane (**coplanar**)
- The halogen and the hydrogen being removed must be **trans** to each other
- Why?
  - Due to **orbital overlap requirements**.
  - In the concerted E2 mechanism, the electrons from the hydrogen must essentially come in **backside** to the leaving halide (**opposite**)
    - just as in backside-attack S<sub>N</sub>2 mechanism



- Sometimes, a molecule will need to single-bond spin into a "trans" conformation to enable a trans-elimination.



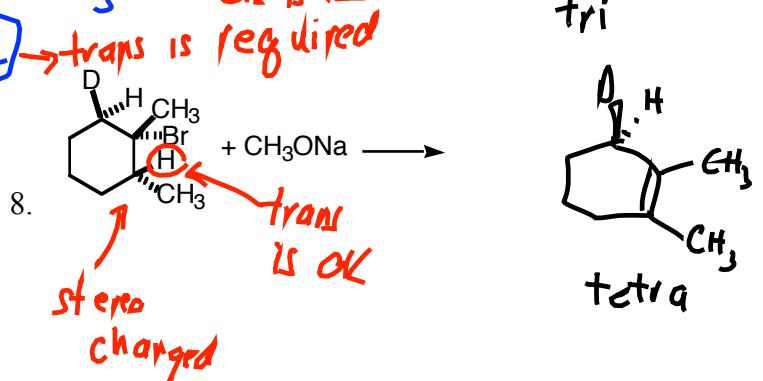
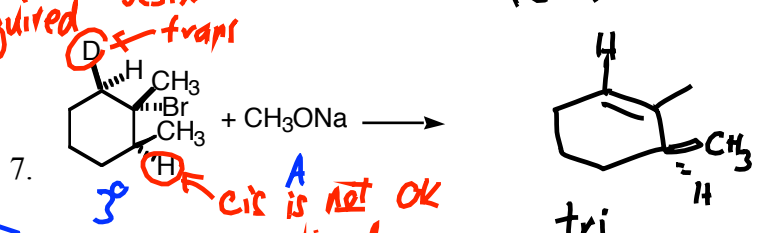
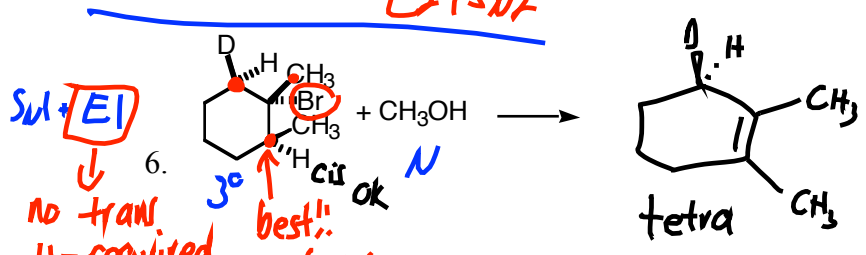
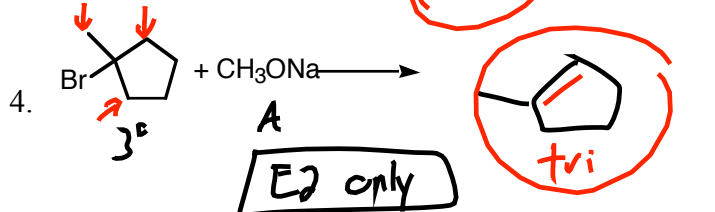
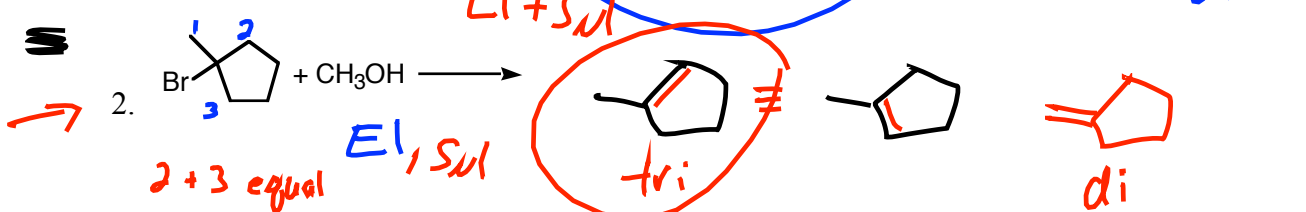
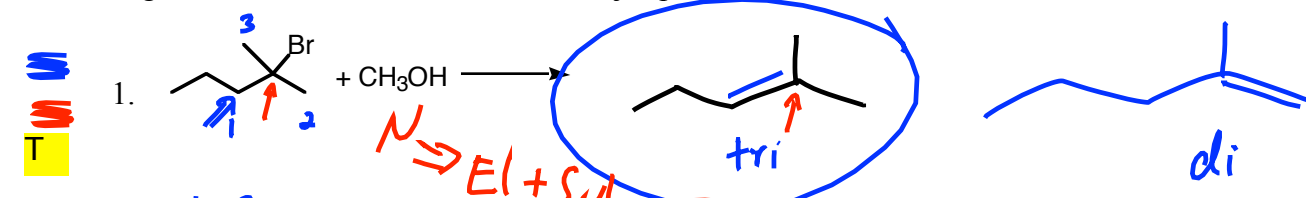
- Eliminations in **Cyclic Compounds** are Often impacted by the Trans Requirement



	E1	E2
1 Nucleophile/Base	Neutral, weak, acidic	Anionic, strong, basic
2 Substrate	1° or 2°	3° RX <del>not allowed</del> E2 3° RX <i>error</i>
Allylic effect...	Allylic Helps	Non-factor
3 Leaving Group	I > Br > Cl	I > Br > Cl
4 Solvent	Polar needed	Non-factor
5 Rate Law	k[RX]	k[RX][Anion]
6 Stereochemistry	Non-selective	Trans requirement
7 Ions	Cationic	Anionic
8 Rearrangements	Problem at times	Never
9 Orientation	Zaitsev's Rule: Prefer more substituted alkene	Zaitsev's Rule: Prefer more Substituted alkene (assuming trans requirement permits)



Elimination Problems: Draw the major Elimination Product for the following Reactions. Classify as E1 or E2. (There may be accompanying S<sub>N</sub>2 or S<sub>N</sub>1 material, but to whatever degree elimination occurs, draw the major product.)



① tetrasubst best  
 ② E1, cis/trans doesn't matter

} Diff product from same reactant, due to E1 vs E2 stereo

} diff. diastereomer reactants gave diff. products

## Comparing $S_N2$ vs $S_N1$ vs E2 vs E1: How Do I Predict Which Happens When?

### Step 1: Check nucleophile/base

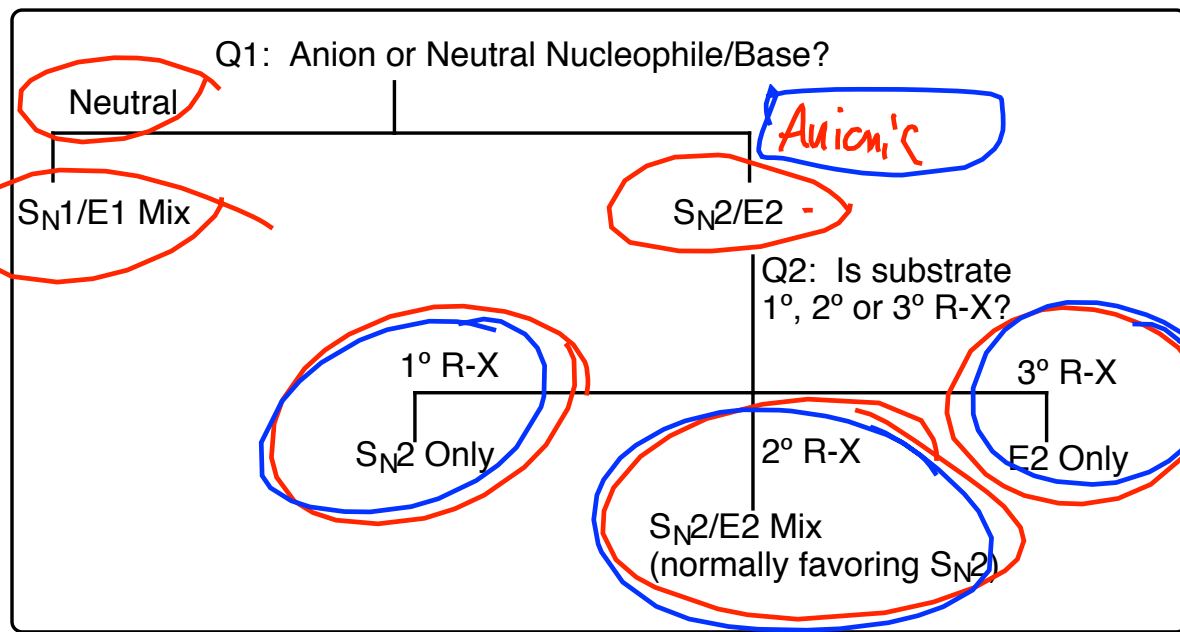
- If **neutral**, then  $S_N1/E1$  → mixture of both
- If **anionic**, then  $S_N2/E2$ .

### Step 2: If **anionic** and in the $S_N2/E2$ pool, then **Check the substrate.**

- $1^\circ \rightarrow S_N2$
- $2^\circ \rightarrow S_N2/E2$  mixture. Often more  $S_N2$ , but not reliable...
- $3^\circ \rightarrow E2$

Notes:

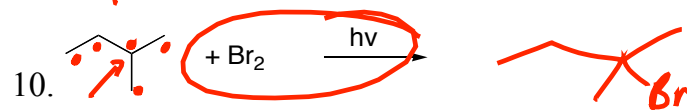
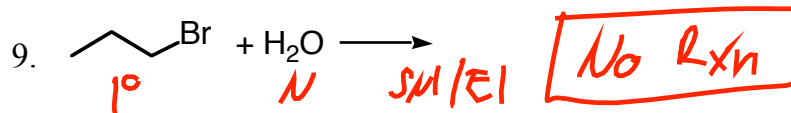
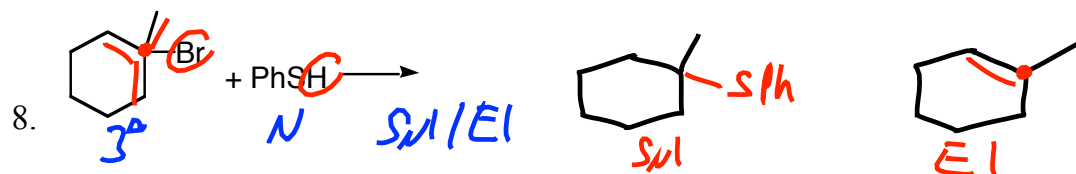
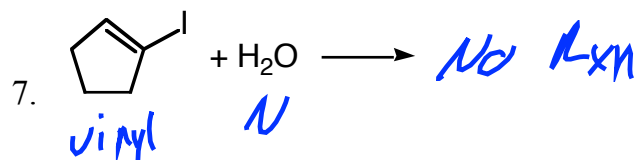
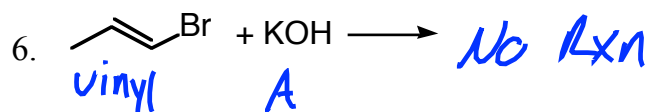
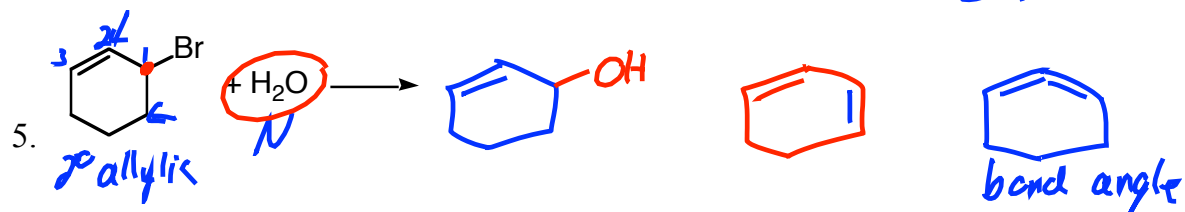
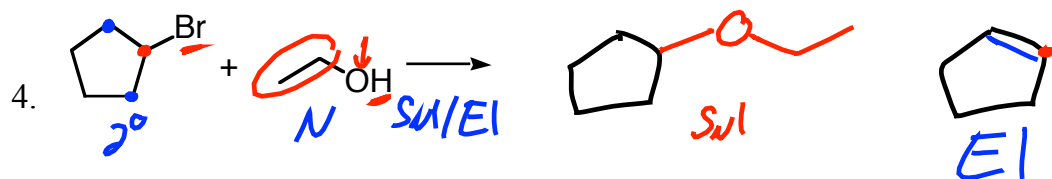
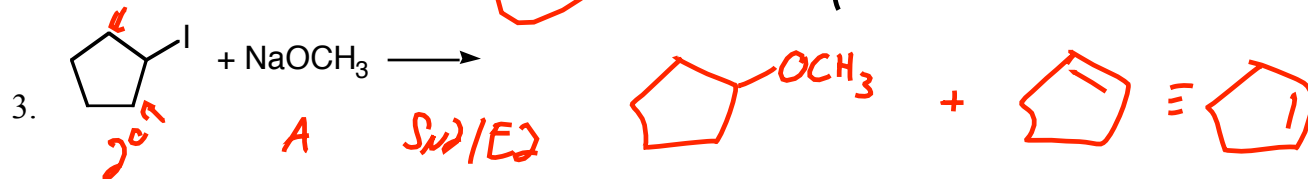
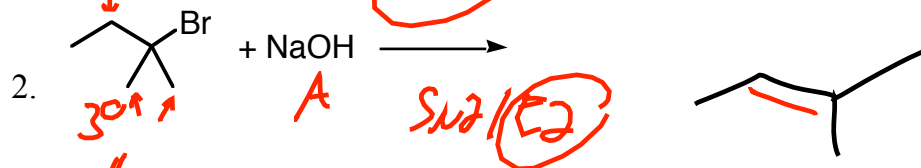
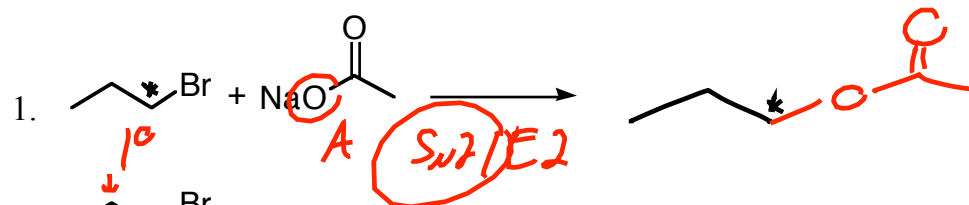
$1^\circ$ R-X	$S_N2$ only	No E2 or $S_N1/E1$ (cation too lousy for $S_N1/E1$ ; $S_N2$ too fast for E2 to compete)
$3^\circ$ R-X	E2 (anionic) or $S_N1/E1$ (neutral/acidic)	No $S_N2$ (sterics too lousy)
$2^\circ$ R-X	mixtures common	



- Note: Aryl and Vinyl Halides will not undergo **any** of these types of reactions.
- If you see  $Br_2/h\nu$  type recipe, then you're back in the chapter 4 world of radical halogenation

For each mixture,

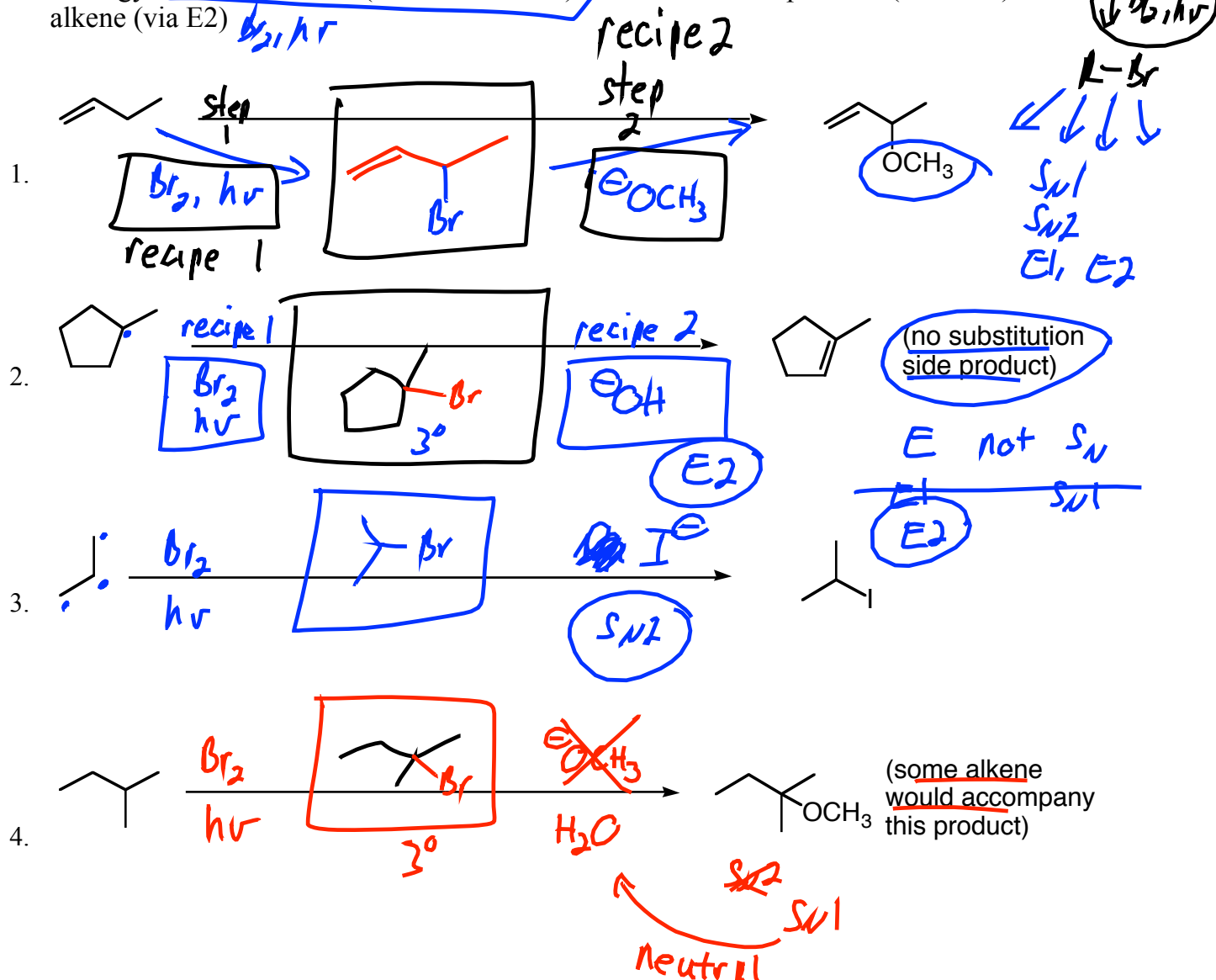
a. Classify the Type of Reaction (or "no reaction")

b. Draw the major product. (Or both a substitution and elim product..)

Rad

## Design Synthetic Plans for converting the starting materials into the target molecules.

- In each case, more than one chemical operation will be required.
- Strategy:  $R-H \rightarrow R-Br$  (via bromination)  $\rightarrow$  Substitution product (via  $S_N2$ ) or alkene (via  $E2$ )



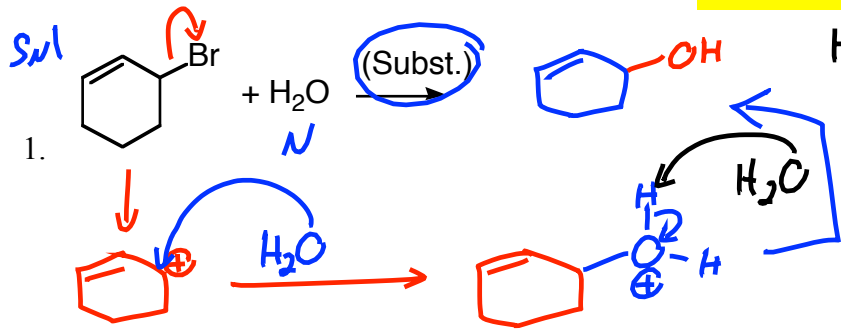
### Keys:

- These can't be done directly, in a single recipe. At least two laboratory operations are required.
- Each sequence show above requires an increase in functional groups. An  $S_N2/S_N1$  or  $E2/E1$  changes functionality but does not create functionality. But radical bromination does create a functional group.
- Thus the key reaction for creating the functionality:  $R-H \xrightarrow{Br_2, h\nu} R-Br$
- Once you've converted the starting alkane to alkyl bromide, you can interconvert that bromide group into something else by  $S_N2/S_N1$  or  $E2/E1$

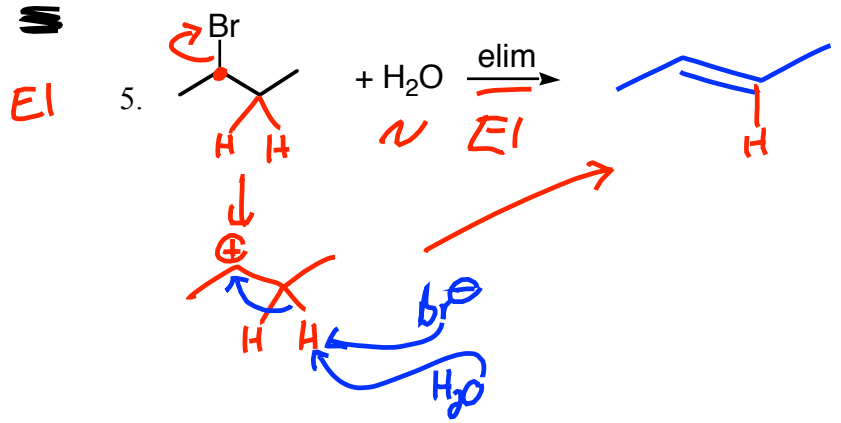
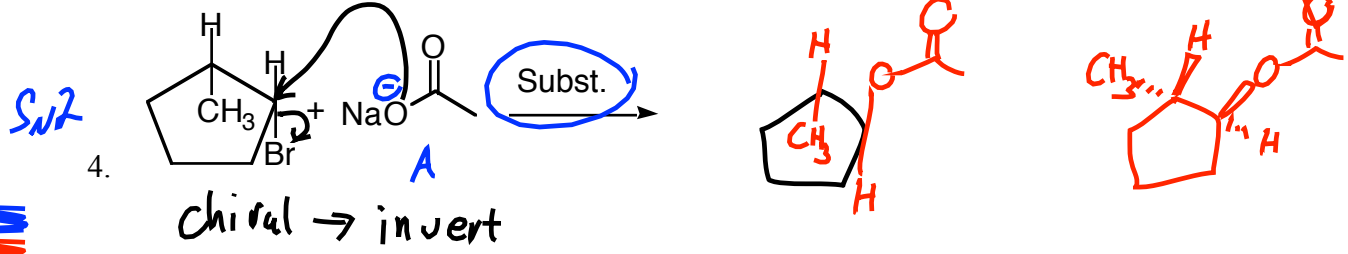
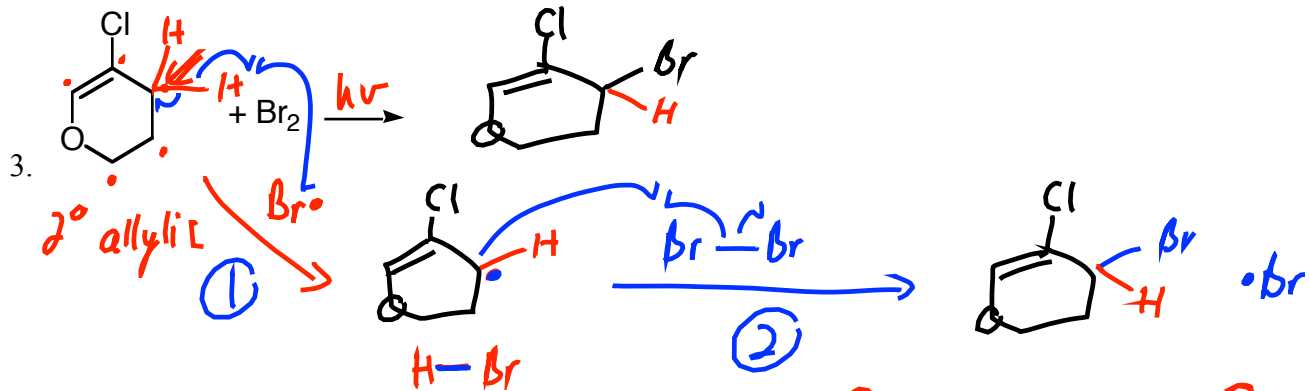
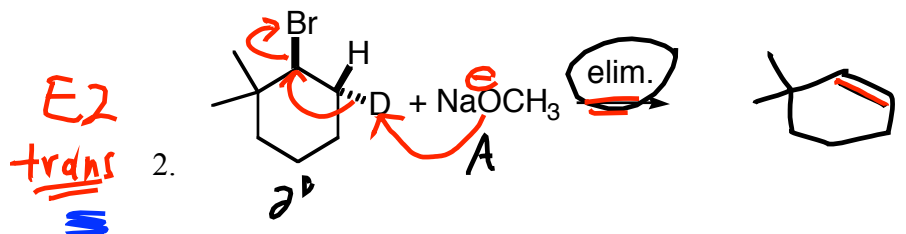
Mechs:  
 Radical halogenation ✓  
 SN2 } anionic  
 E2 }  
 SN1 } cationic  
 E1 }  
 S<sub>N</sub>1

**Practice: Mechanism Practice**

Draw the **mechanism** for formation of the major products in the following reactions. In some cases where both elimination and substitution are possible, the problem specifies whether to draw the substitution or elimination product.



Deprot (in an SN1 or an E1)  
 1. No base shown  
 2. Bromide anion as base  
 3. Solvent molecule as base



**Practice: Ranking Practice**

Rank the Reactivity of the chemicals shown toward the thing in the box. **Keys:**

- Identify the type of reaction that would be involved
- Think about the rate-determining step and how reactant or product or transition-state stability would influence the rate.

**1. Neutral**

Reaction:  $R-X \rightarrow R^{\oplus} + X^{\ominus}$

Reagents:  $Li^+$ ,  $Na^+$ ,  $K^+$ ,  $T^+$ ,  $M^+$

Substrate: CCC(=O)O

Options: CC(Br)C=C (1), CC(Br)C=C (4), CC(Br)CC=C (2), CC(Br)C (2)

Handwritten notes:  $2^{\circ}$  allylic, vinyl,  $1^{\circ}$ ,  $2^{\circ}$

**2. Radical**

Reaction:  $R-H \xrightarrow{Br_2, hv} R^{\bullet} + HBr$

Reagents:  $Li^+$ ,  $Na^+$ ,  $K^+$ ,  $T^+$ ,  $M^+$

Substrate: Br2, hv

Options: H3C-CH3 (3), CC(C)C (2), CC=CC (1)

Handwritten notes:  $H_3C-CH_2$  ( $1^{\circ}$ ),  $2^{\circ}$ ,  $2^{\circ}$  allylic

**3.  $R-H + X^{\bullet} \rightarrow R^{\bullet} + H-X$**

Reagents:  $Li^+$ ,  $Na^+$ ,  $K^+$ ,  $T^+$ ,  $M^+$

Substrate: CC(C)C

Options: Cl^{\bullet} (1), Br^{\bullet} (2), I^{\bullet} (3)

Handwritten notes: least stable (as radicals), most stable, most stable,  $R-Cl$ ,  $R-Br$ ,  $R-I$

**4.  $Nu^-$  reactant**

Reaction:  $R-X \xrightarrow{Nu^-} R-Nu + X^-$

Reagents:  $Li^+$ ,  $Na^+$ ,  $K^+$ ,  $T^+$ ,  $M^+$

Substrate: CC(C)I

Options: CH3OH (3), CC(=O)O^- Na^+ (2), CC(O^-)Na^+ (1)

Handwritten notes: Stability, reactivity, 1 neut, res

**5.  $(S_N1)$**

Reaction:  $R-X \rightarrow R^{\oplus} + X^{\ominus}$

Reagents:  $Li^+$ ,  $Na^+$ ,  $K^+$ ,  $T^+$ ,  $M^+$

Substrate: CC(C)(C)Br

Options: CH3OH (3), CC(=O)C (2), H2O (1)

Handwritten notes: Solvent: Pentane

**6. Anion**

Reaction:  $R-X + OH^- \rightarrow R-OH + X^-$

Reagents:  $Li^+$ ,  $Na^+$ ,  $K^+$ ,  $T^+$ ,  $M^+$

Substrate: NaOH

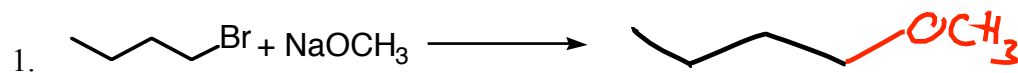
Options: CC(C)I (1), CC(C)C (2), CC(C)Br (3)

Handwritten notes:  $1^{\circ} > 2^{\circ}$ ,  $I > Br$

**Practice: Predict-the-Product Practice**

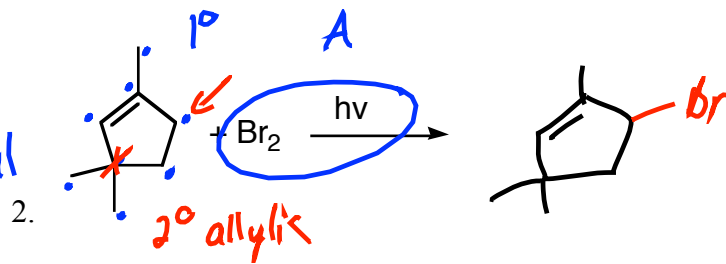
Give the Major Product(s) for each of the following. If it's likely to give a mixture of both substitution and elimination, just draw the substitution product. Designate stereochemical outcomes when stereochemistry is relevant ( $2^\circ$  substrates).

Key: Try to recognize what type of reaction will happen first.



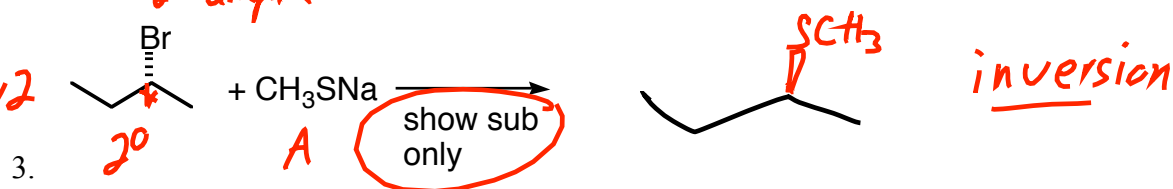
*S<sub>N</sub>2*

radical



2.

*2° allylic*



*S<sub>N</sub>2*

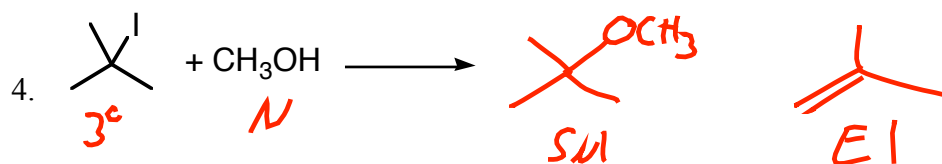
3.

*2°*

show sub only

*inversion*

*S<sub>N</sub>1/E1*



4.

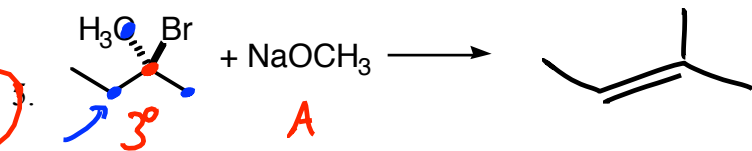
*3°*

*N*

*S<sub>N</sub>1*

*E1*

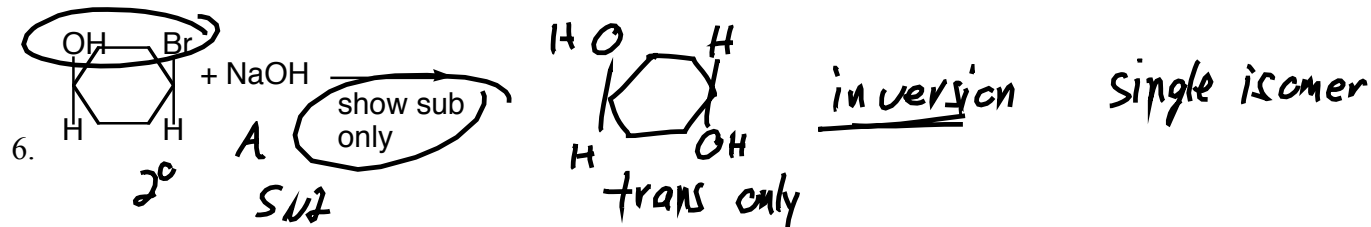
*S<sub>N</sub>2/E2*



5.

*3°*

*A*



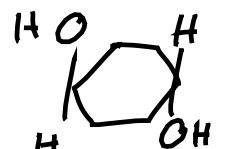
6.

*2°*

*A*

show sub only

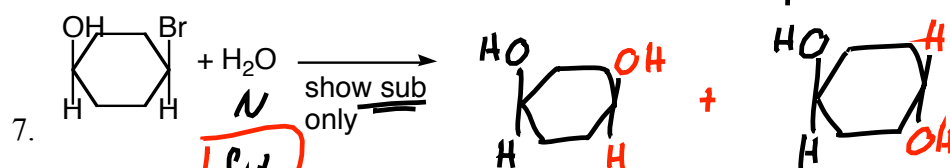
*S<sub>N</sub>2*



*trans only*

*inversion*

*single isomer*

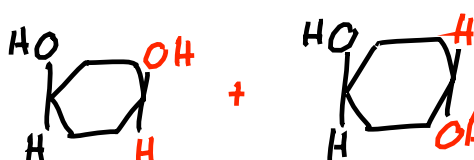


7.

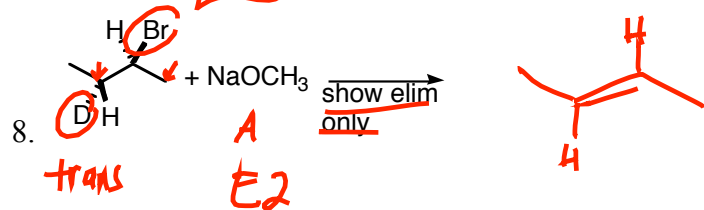
*N*

show sub only

*S<sub>N</sub>1*



*two isomers*  
*cis + trans*



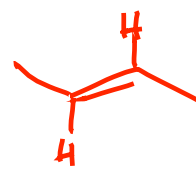
8.

*trans*

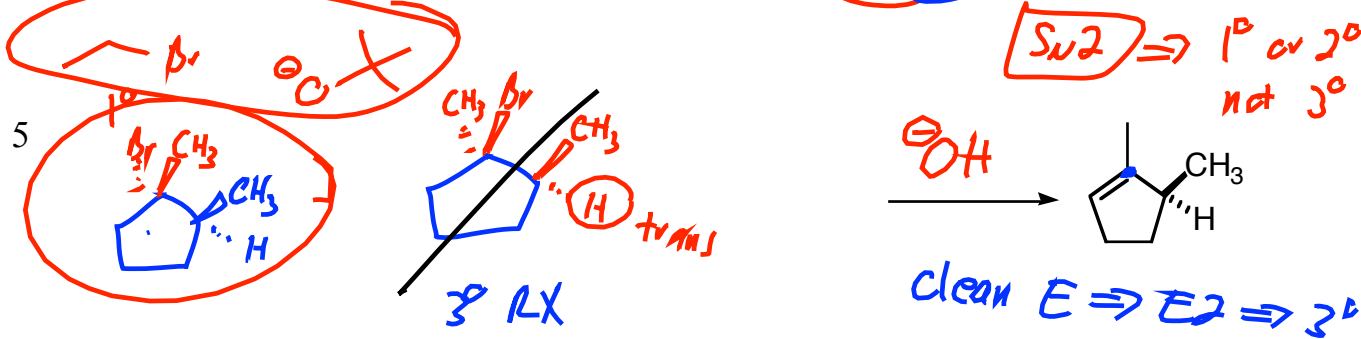
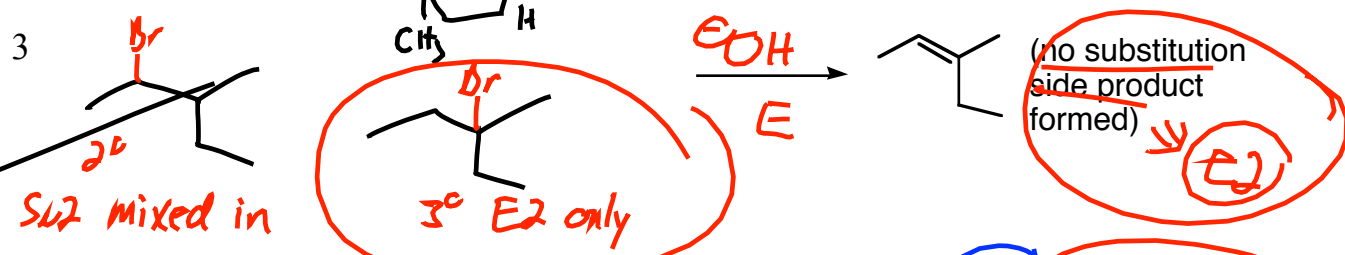
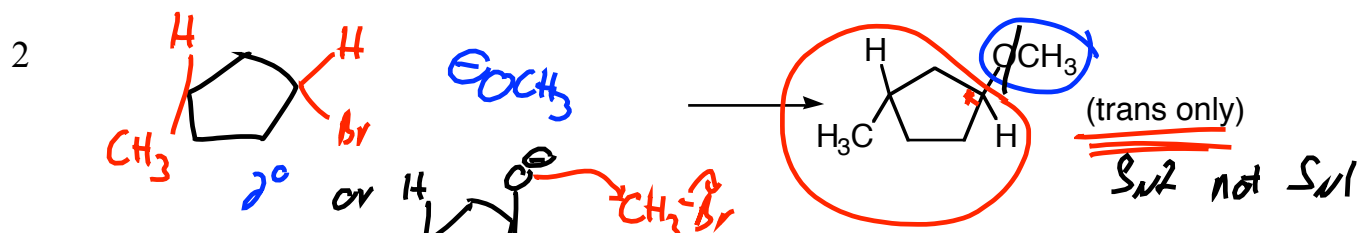
*A*

show elim only

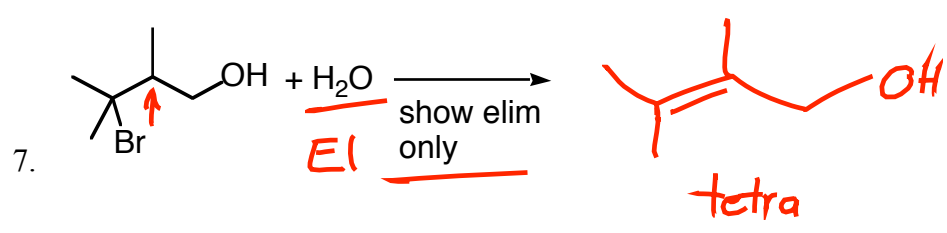
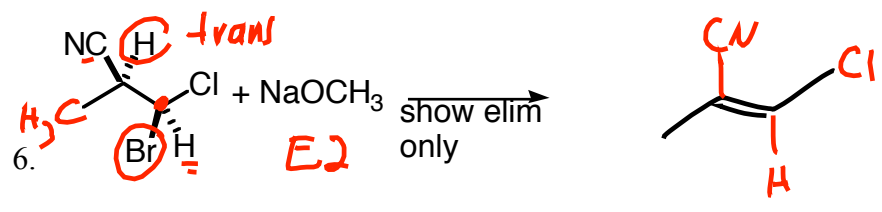
*E2*



Provide Reactants for the Following (One of the Starting Chemicals must be an R-Br)



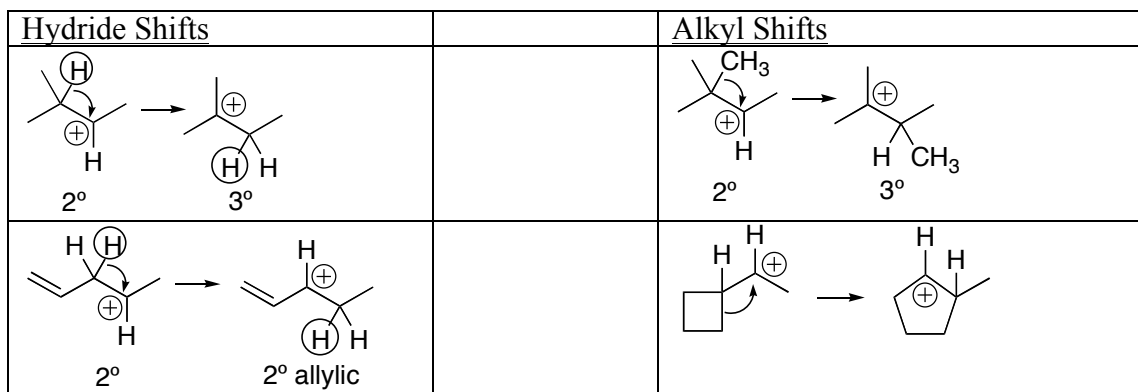
Draw the Major Alkene Isomer, Following Elimination



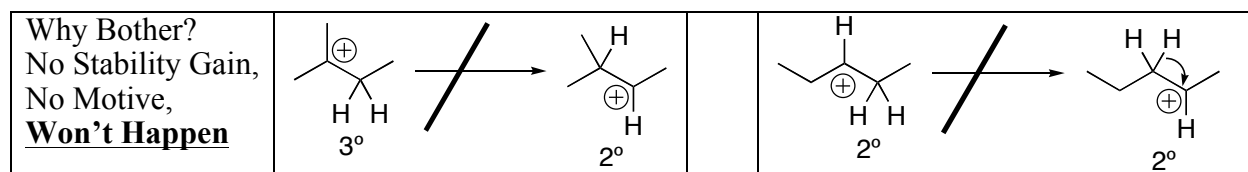
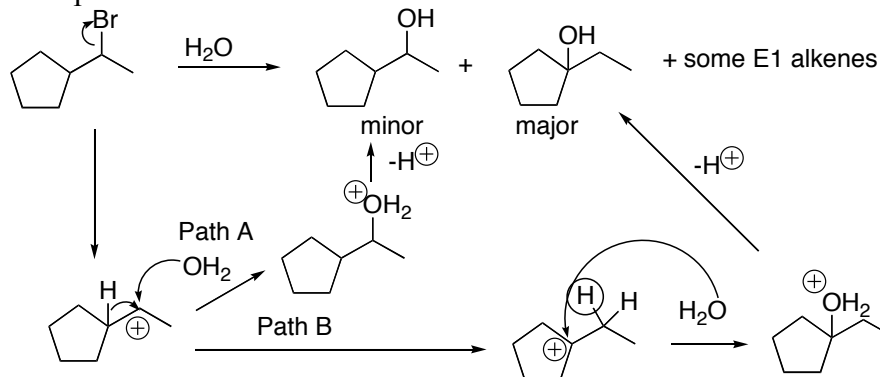


6-15 **Carbocation Rearrangements** (and their impact in  $S_N1$  and E1 reactions)

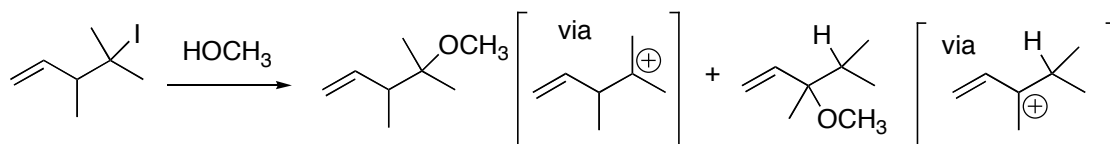
1. Carbocations are very unstable, and sometimes rearrange to other more stable carbocations.
2. A rearrangement requires that a superior cation will result. Four cases:
  - a.  $2^\circ \rightarrow 3^\circ$
  - b. non-allylic  $\rightarrow$  allylic
  - c. strained ring  $\rightarrow$  unstrained or less strained ring
  - d.  $1^\circ$  cation  $\rightarrow$   $2^\circ$  or  $3^\circ$  cation (rare, since  $1^\circ$  cations are hard to make and pretty rare)



3. Two processes for cation rearrangement:
  - a. Hydride shift (an H jumps over)
  - b. Alkyl shift (a carbon jumps over)
    - The resulting cation must always be on a carbon adjacent to the original
    - rearrangement does not occur if you start with a good cation.
4. Most cation mechanisms that start with  $2^\circ$  or  $3^\circ$  cations don't undergo rearrangement because rearrangement does not lead to improved cation stability

5. Examples in  $S_N1$ 

- Product mixture results from competition between Path A and Path B.



W  
W  
W  
W

W  
W  
W  
W

W  
W  
W  
W